In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: September 23, 2022

MISTY PASCO, *parent and next friend of M.P., a minor*,	*	No. 16-500V
Petitioner,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Measles-Mumps-Rubella Vaccine; Varicella Vaccine; Acute Disseminated Encephalomyelitis ("ADEM"); Transverse Myelitis ("TM"); Substantial Factor
Respondent.	*	

Richard Gage, Richard Gage, P.C., Cheyenne, WY, for Petitioner.
Tyler King, United States Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

On April 22, 2016, Misty Pasco ("Petitioner") filed a petition for compensation on behalf of her minor child M.P. pursuant to the National Vaccine Injury Compensation Program.[2] Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to -34 (2012). Petitioner alleges that the measles-mumps-rubella ("MMR") and varicella vaccines M.P. received on May 14, 2015, caused her to suffer from transverse myelitis ("TM").[3] Pet. at 1–2. Petitioner filed an amended petition on January 30, 2018, alleging that M.P.'s May 14, 2015 vaccinations were the cause-in-fact of her TM and acute

[1] This Ruling shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted Ruling. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

[3] Transverse myelitis ("TM") is "myelitis in which the functional effect of the lesions spans the width of the entire cord at a given level." *Dorland's Illustrated Medical Dictionary* 1, 1218 (32nd ed. 2012) [hereinafter "*Dorland's*"]. Myelitis is "inflammation of the spinal cord[.]" *Dorland's* at 1218.

disseminated encephalomyelitis ("ADEM").[4] Am. Pet. at 2, ECF No. 52. Petitioner further alleges that M.P.'s vaccinations caused the Table injury of encephalitis.[5] *Id.*

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,[6] I find that Petitioner has provided preponderant evidence that the MMR and varicella vaccines M.P. received on May 14, 2015, were the cause-in-fact of her TM and ADEM. However, in light of M.P.'s ADEM diagnosis, Petitioner has failed to satisfy her burden for her Table claim of encephalitis. Accordingly, Petitioner is entitled to compensation and this case shall proceed to the damages phase.

I. Procedural History

Petitioner filed her petition for compensation on April 22, 2016. Pet. at 1. On May 6, 2016, Petitioner filed M.P.'s medical records and a statement of completion. Pet'r's Exs. 1–14, ECF Nos. 9-1–11-6, 12.[7] Petitioner filed additional medical records on July 6 and 18, 2016. Pet'r's Exs. 15–16, ECF Nos. 17–18.

Respondent filed his Rule 4(c) report on August 5, 2016, recommending that compensation be denied. Resp't's Report at 1, ECF No. 19. Petitioner filed an additional medical record on August 8, 2016. Pet'r's Ex. 17, ECF No. 20-1. The presiding special master held a status conference pursuant to Vaccine Rule 5 on August 9, 2016. *See* Min. Entry, docketed Aug. 10, 2016. Following the status conference, the presiding special master ordered Petitioner to file an expert report on causation that "address[ed] the lingering concerns about potential alternative causes of [M.P.'s] alleged condition." Sched. Order at 1, ECF No. 21. Prior to filing an expert report, Petitioner submitted M.P.'s vaccination record on August 30, 2016. Pet'r's Ex. 18, ECF No. 22-1.

On January 4, 2017, Petitioner filed an expert report from Lawrence Steinman, M.D. Pet'r's Exs. 19–20, ECF Nos. 30-1–30-2. This case was reassigned to me on January 9, 2017. ECF Nos. 31–32. Respondent filed a responsive expert report from Hayley Gans, M.D., along with supporting medical literature, on May 2, 2017. Resp't's Exs. A–B, A Tabs 1–18, ECF Nos. 35-1–

[4] Acute disseminated encephalomyelitis ("ADEM") is "an acute or subacute encephalomyelitis or myelitis characterized by perivascular lymphocyte and mononuclear cell infiltration and demyelination; it occurs most often after an acute viral infection, especially measles, but may occur without a recognizable antecedent. It is believed to be a manifestation of an autoimmune attack on the myelin of the central nervous system. Symptoms include fever, headache, and vomiting; sometimes tremor, seizures, and paralysis; and lethargy progressing to coma that can be fatal. Many survivors have residual neurologic deficits." *Dorland's* at 613.

[5] Encephalitis is generally "inflammation of the brain." *Dorland's* at 612.

[6] While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("Finding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

[7] Petitioner's original exhibit number 8 was stricken from the record and a corrected version was re-filed on December 13, 2016. *See* Pet'r's Ex. 8, ECF No. 27-1; *see also* ECF Nos. 25–26.

35-2, 36–37. The following day, Respondent filed an additional expert report from Michael Kruer, M.D. Resp't's Exs. C–D, ECF Nos. 38-1–38-2. Respondent filed supporting medical literature on June 16, 2017. Resp't's Exs. C Tabs 1–14, ECF Nos. 40-1–41-10.

I held a status conference with the parties on July 11, 2017. *See* Min. Entry, docketed July 11, 2017. Following the status conference, I ordered Petitioner to file a responsive supplemental expert report specifically "addressing th[e] alternative cause[]" in this case. Sched. Order at 1, ECF No. 44. Petitioner submitted a supplemental expert report and supporting medical literature on November 2, 2017. Pet'r's Exs. 21–25, ECF Nos. 46-1–46-5. The same day, I ordered Respondent to file his responsive supplemental expert reports. Non-PDF Order, docketed Nov. 2, 2017. Following one extension of time, Respondent filed a motion to stay the filing of his responsive supplemental expert reports on the basis that the Department of Health and Human Services was awaiting an appropriation from Congress. ECF Nos. 47–48. Appropriations were restored the same day that Respondent's motion was filed, and I therefore denied Respondent's motion on January 23, 2018. ECF No. 49. The same day, Respondent filed his responsive supplemental expert reports. Resp't's Exs. E, E Tab 1, F, ECF Nos. 50-1–50-3.

On January 29, 2018, I held a status conference with the parties. *See* Min. Entry, docketed Jan. 29, 2018. During the status conference, the parties discussed the legal burden applicable to claims, such as Petitioner's, in which there is a dispute concerning competing causes. Sched. Order at 1, ECF No. 51. Petitioner noted she planned to file an amended petition alleging that M.P. suffers from ADEM, "which is a form of encephalitis." *Id.* The parties agreed that M.P.'s ADEM and human metapneumovirus ("HMPV") infection[8] diagnoses were not in dispute. *Id.* Petitioner explained that at the time the original petition was filed, the Program "regularly treated ADEM as a [T]able injury when pled as encephalitis." *Id.* at 2. Petitioner "acknowledged that ADEM is now among the exclusionary criteria for encephalitis in the [Table]." *Id.* Petitioner filed an amended petition on January 30, 2018, alleging that M.P. suffers from TM, ADEM, and Table encephalitis. Am. Pet., ECF No. 52.

In response to Petitioner's amended petition, Respondent filed a status report stating his position on March 5, 2018. ECF No. 53. Specifically, Respondent argued that Petitioner failed to establish a Table claim for encephalopathy or an ADEM/TM causation-in-fact claim, and Respondent requested that this matter be scheduled for an entitlement hearing. *Id.* Petitioner filed a response on April 7, 2018, arguing that the evidence supports her claim. *See* ECF Nos. 54–55. Two days later, Petitioner filed additional medical literature. Pet'r's Exs. 26–32, ECF Nos. 56-1–56-7. Petitioner filed an affidavit on April 16, 2018. Pet'r's Ex. 33, ECF No. 57-1.

The following day, on April 17, 2018, I held a status conference with the parties. *See* Min. Entry, docketed Apr. 17, 2018. During the conference, I indicated that "the medical records do not seem to support an encephalitis/encephalopathy [T]able injury." Sched. Order at 1, ECF No. 58. Petitioner indicated that she wished to proceed on her causation-in-fact claim. *Id.* The parties

[8] A human metapneumovirus ("HMPV") infection is "a species that causes respiratory infection in humans that is clinically similar to, but less severe than, that caused by respiratory syncytial virus." *Dorland's* at 1144. Respiratory syncytial virus ("RSV") refers to "any of a group of viruses belonging to the genus *Pneumovirus,* isolated originally from chimpanzees . . . . In humans, they cause respiratory disease that is particularly severe in infants, in whom it causes bronchiolitis [] and sometimes pneumonia." *Id.* at 2064.

reiterated that they do not dispute M.P.'s ADEM or HMPV infection diagnosis, or the timing of her symptoms. *Id.* They also maintained that the main issue in this case is "a legal question concerning the burdens relating to whether the viral infection or the vaccinations caused [M.P.'s] injuries." *Id.* Following the status conference, I ordered the parties to file briefs articulating their positions on the legal burdens applicable to this case. *Id.* at 2. The parties filed simultaneous memoranda regarding their legal burdens on August 13, 2018. Pet'r's Mem., ECF No. 61; Resp't's Mem., ECF No. 62.

While awaiting an entitlement hearing, Petitioner filed an updated medical record on December 27, 2019. Pet'r's Ex. 34, ECF No. 64-1. On August 19, 2020, Petitioner filed a notice of additional authority regarding her legal burden. ECF No. 65. I scheduled this matter for an entitlement hearing to take place on June 2–3, 2021. Hearing Order, ECF No. 69. The parties relied on their previously filed memoranda in place of pre-hearing briefings. Pre-Hearing Order, ECF No. 70. The entitlement hearing was held remotely as scheduled on June 2, 2021. *See* Min. Entry, docketed June 2, 2021. Following the entitlement hearing, Petitioner filed a status report indicating that she did not wish to file post-hearing briefings and requesting I issue a Decision based on the existing record. ECF No. 80. This matter is now ripe for consideration.

II. Factual Background

A. Medical Records

M.P. was born full-term on May 8, 2014, and was healthy at birth. Pet'r's Ex. 3 at 1, ECF No. 9-3. M.P. had normal newborn examinations *Id.* at 6. During M.P.'s well-child visits during her first year, Petitioner requested that M.P. receive her vaccinations on a modified schedule of two per visit. *See* Pet'r's Ex. 4, ECF No. 9-4. M.P. did not experience adverse reactions to her scheduled vaccinations in the first twelve months of her life. *See id.*

On May 5, 2015, M.P. presented to Phoenix Indian Medical Center ("PIMC"), her primary care provider, for persistent ear pain. *Id.* at 43. Petitioner reported that M.P. had gone to urgent care on April 15, 2015, and was diagnosed with otitis media ("OM")[9] and prescribed amoxicillin.[10] *Id.* M.P. presented to PIMC for her twelve-month well-child visit on May 14, 2015. *Id.* at 49. Petitioner noted "no concerns" regarding M.P. *Id.* M.P.'s examination was normal, and she received the MMR and varicella vaccinations during this visit. *Id.* at 51–53.

One week later, on May 21, 2015, M.P. returned to Dr. Bernadette Freeland-Hyde at PIMC with symptoms of fever, cough, and congestion that began three days prior (four days post

[9] Otitis media is "inflammation of the middle ear; subtypes are distinguished by length of time from onset *(acute* versus *chronic)* and by type of discharge *(serous* versus *suppurative).*" *Dorland's* at 1351.

[10] Amoxicillin is "a semisynthetic derivative of ampicillin effective against a broad spectrum of gram-positive and gram-negative bacteria; used especially in the treatment of infections due to susceptible strains of *Haemophilus influenzae, Escherichia coli, Proteus mirabilis, Neisseria gonorrhoeae,* streptococci (including *Streptococcus faecalis* and *S. pneumoniae*), and non-penicillinase-producing staphylococci." *Dorland's* at 65.

vaccination). *Id.* at 55. Her examination showed bilateral bulging tympanic membranes,[11] teary discharge, and a low-grade fever of 99 degrees Fahrenheit. *Id.* at 55–56. M.P.'s pediatrician diagnosed her with bilateral OM and prescribed antibiotics. *Id.* On May 25, 2015, Petitioner took M.P. to the emergency room ("ER") with complaints of continued fevers. *Id.* at 57. Her temperature was 102.6 degrees Fahrenheit. *Id.* Petitioner reported that M.P.'s fever had resolved the day after being diagnosed with OM but then had returned later that same day, along with vomiting and "loose stools." *Id.* Regarding M.P.'s "loose stool[,]" her pediatrician noted that M.P. was taking antibiotics for her OM. *Id.* The examination of M.P.'s ears, nose, and throat revealed normal bilateral tympanic membranes and no rhinorrhea or nasal drainage. *Id.* at 65. Her neurological examination was normal. *Id.* The attending physician diagnosed M.P. with a fever, vomiting, bilateral OM, and an insect bite on her right thigh. *Id.* at 66. The physician prescribed acetaminophen (Tylenol) and Azithromycin,[12] and M.P. received an injection of Ceftriaxone.[13] *Id.*

The next day, on May 26, 2015, M.P. returned to her pediatrician's office. *Id.* at 76. Petitioner reported that M.P.'s fever, diarrhea, and vomiting had resolved, but Petitioner expressed concerns over M.P.'s poor oral intake. *Id.* M.P.'s pediatrician recommended fluids and to follow up in one day. *Id.* at 77.

On May 27, 2015, M.P. followed up with her pediatrician "for prolonged weakness." *Id.* at 80. Petitioner reported that M.P. still had poor oral intake, was very weak, and was "refusing to walk[.]" *Id.* Her pediatrician noted a "6.5[%] weight loss since [May 21, 2015.]" *Id.* An examination of M.P. revealed that she was alert and responsive but exhibited hypotonia[14] and lethargy. *Id.* at 81. M.P.'s pediatrician referred her to the ER. *Id.* M.P.'s ER examination showed that she was alert but had diminished strength. Pet'r's Ex. 5 at 6, ECF No. 10-1. The attending physician admitted M.P. for dehydration. *Id.* at 8. Petitioner reported that "around the 25th or 26th [of May,]" M.P. had not been using her upper extremities and "she seemed tired and weak overall." *Id.* at 18. A respiratory panel was positive for HMPV and M.P.'s urinalysis was concerning for a UTI. *Id.*

M.P. underwent a neurological examination on May 29, 2015, which showed that she was irritable, crying, had poor neck control, and exhibited little movement in her lower extremities. *Id.* at 33. An MRI of the brain and spinal cord on May 30, 2015, revealed "longitudinal myelitis." *Id.*

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[11] Tympanic membranes are also called "membrana tympanica" or "eardrums." They are "the obliquely placed, thin membranous partition between the external acoustic meatus and the tympanic cavity. The greater portion, the pars tensa, is attached by a fibrocartilaginous ring to the tympanic plate of the temporal bone; the much smaller, triangular portion, the pars flaccida, is situated anterosuperiorly between the two malleolar folds." *Dorland's* at 1128.

[12] Azithromycin is "an antibiotic, derived from erythromycin, that inhibits bacterial protein synthesis, effective against a wide range of gram-positive, gram-negative, and anaerobic bacteria; used in the treatment of mild to moderate infections caused by susceptible organisms, administered orally and intravenously." *Dorland's* at 187.

[13] Ceftriaxone sodium is "a semisynthetic, β-lactamase–resistant, broad-spectrum, third-generation cephalosporin effective against a wide range of gram-positive and gram-negative bacteria; administered intravenously or intramuscularly." *Dorland's* at 312.

[14] Hypotonia is "a condition of diminished tone of the skeletal muscles, so that they have diminished resistance to passive stretching and are flaccid; this usually means the nerve supply is compromised." *Dorland's* at 907.

at 18. The impression of M.P.'s MRI was a "symmetric, central increased T2 signal of the cord extending from the cranio-cervical junction to T10." *Id.* at 162. The MRI also showed "[l]ong segment cord signal abnormality . . . with vague cord enhancement." *Id.* Such findings were "most consistent with [ADEM]." *Id.* A lumbar puncture performed to collect cerebrospinal fluid ("CSF") revealed elevated white blood cells, but normal red blood cells, protein, and glucose. *Id.* at 41, 163. M.P. was assessed with "longitudinally extensive transverse myelitis[.]" *Id.* at 41. M.P. received IV steroids and IVIG for four days with a plan to continue oral steroids for three to four weeks "and then slowly taper over another [four] weeks" following discharge. *Id.* at 35, 41. A note from the attending neurologist dated June 2, 2015, indicated that M.P. "had a history of recent vaccination and [a] possible viral infection." *Id.* at 33. M.P. was discharged on June 6, 2015, with a full range of motion ("ROM") of her upper extremities and right lower extremity. *Id.* at 24. She still had fine motor deficits and was unable to crawl. *Id.*

On June 8, 2015, M.P. returned to her pediatrician for a follow-up. Pet'r's Ex. 10 at 23, ECF No. 11-2. Petitioner reported that M.P. was irritable the day before. *Id.* Upon examination, M.P. was alert but still had motor deficits. *Id.* Her pediatrician noted that the "etiology is unclear as [M.P.] tested positive for [an HMPV infection] and also received the MMR/varicella vaccines about [one and a half] weeks prior to the onset of [her] symptoms." *Id.* The pediatrician's assessment of M.P. included a "fussy baby from post hospitalization from transverse myelitis – unclear if [M.P.] is in pain from [the] high dose of prednisolone or from myelitis." *Id.* at 24.

M.P. followed up with neurologist Vinodh Narayanan, M.D., on June 12, 2015. Pet'r's Ex. 15 at 1, ECF No. 17-1. Dr. Narayanan noted that M.P. had TM and "perhaps subtle features of ADEM." *Id.* Upon examination, M.P. was unable to sit by herself, and her left ankle was tight. *Id.* Dr. Narayanan noted that M.P. was otherwise alert, smiling, and interactive. *Id.* His plan was to continue tapering her prednisolone. *Id.* M.P. had another follow up with Dr. Narayanan on June 17, 2015. *Id.* at 6. He noted that M.P. was improving with physical therapy ("PT"). *Id.* An examination revealed tight heels. *Id.*

From June 24 to December 23, 2015, M.P. received treatment with PT. Pet'r's Ex. 11 at 1, ECF No. 11-3. The note from her initial appointment on June 24, 2015, indicates that M.P.'s TM and ADEM diagnosis "ha[d] possibly been linked to [the] MMR [vaccine she] received [eleven] days prior to her hospitalization." *Id.* The physical therapist noted that M.P. was "regaining the ability to prop sit but [wa]s dependent for mobility." *Id.*

M.P. returned to Dr. Narayanan for a follow-up on August 25, 2015. Pet'r's Ex. 15 at 2. He noted that M.P. was "now completely done with her steroid taper." *Id.* He also noted that Petitioner started M.P. in hyperbaric oxygen[15] and acupuncture therapies. *Id.* Upon examination, Dr. Narayanan indicated that M.P. was "able to stand and walk on a broad[-]based gait[, s]he circumducts [sic] the left leg, and has some genu recurvatum[16] on the left." *Id.* He further noted that M.P. exhibited diminished tone in her legs and "w[ould] lose her balance and fall

[15] Hyperbaric oxygen treatment is "exposure of a patient to oxygen under pressure greater than normal atmospheric pressure, done for individuals who need more oxygen than they can take in by breathing in the normal atmosphere or with an oxygen mask." *Dorland's* at 1356.

[16] Genu recurvatum refers to the "hyperextension of the knee; called also back knee." *Dorland's* at 771.

periodically." *Id.* His impression of M.P. was "resolving symptoms of myelitis" and he recommended continued PT. *Id.*

On December 8, 2015, M.P. returned to Dr. Narayanan for a follow-up. *Id.* at 3. Dr. Narayanan noted that M.P. was "making steady progress in her motor skills[]" but that "[h]er speech development ha[d] been a bit slow." *Id.* He wrote that M.P. was also being treated by a naturopathic physician, "who ordered [a] hair analysis for heavy metals." *Id.* Dr. Narayanan noted that M.P.'s hair analysis showed elevated iodine and uranium. *Id.* He indicated that he was "not sure how to interpret this test result and [] referred [Petitioner] back to [the] naturopathic physician." *Id.*

M.P. underwent a speech evaluation on December 16, 2015. Pet'r's Ex. 11 at 28. The evaluation revealed that both M.P.'s receptive and expressive language scores fell below average for her age. *Id.* However, the evaluator noted that M.P. appeared to have improved language skills each week and did not qualify for speech services. *Id.* By the end of M.P.'s PT treatment on December 23, 2015, the physical therapist noted that M.P. still had significant motor skill delay due to her acute TM diagnosis. *Id.* at 36.

M.P. attended additional PT throughout 2016. Pet'r's Ex. 34 at 35, ECF No. 64-1. On November 8, 2016, M.P.'s physical therapist told Petitioner that M.P. could benefit from orthotic braces[17] to correct the pronation[18] in her legs. *Id.* M.P. presented to podiatrist Ana Burns, D.P.M., for orthotics on November 23, 2016. *Id.* at 33. During this visit, Petitioner reported that M.P. experienced pain in her lower extremities at nighttime after running and jumping during the day. *Id.*

On February 8, 2017, M.P. returned to Dr. Burns for a follow-up. *Id.* at 28. Dr. Burns noted that M.P. exhibited "[bilateral lower extremity] weakness[,] gait abnormality[, and] pronation" with a slight foot drag on her right side. *Id.* at 28, 30. She wrote that "[M.P.] has [a history] of [TM] from vaccination which resulted in [bilateral lower extremity] weakness." *Id.* at 29. Dr. Burns noted that such conditions improved with arch supports. *Id.* at 30. She also ordered M.P. to continue her strengthening exercises. *Id.* Dr. Burns noted that M.P. wears athletic shoes with her issued orthotics. *Id.* at 29. Petitioner reiterated that M.P. would cry after running all day and described the pain as a 7/10. *Id.* Dr. Burns recommended ibuprofen (Advil) for the pain. *Id.*

Over a year later, on June 12, 2018, M.P. presented for a neurology follow-up. *Id.* at 27. The physician noted that M.P. exhibited "paresthesias of the skin [especially] in the legs." *Id.* Upon examination, M.P. did not show any "features of a peripheral neuropathy." *Id.* The physician noted her opinion that "it was unlikely that [M.P.'s] new sensory symptoms [were] connected with the

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[17] Orthotic braces are also called "supra-malleolar orthosis," which "support[] the leg just above the anklebones or malleoli." Scheck & Siress, *SMO (Supra-Malleolar Orthosis),* PROSTHETICS, ORTHOTICS, PEDORTHICS https://www.scheckandsiress.com/wp-content/uploads/2016/08/SMO-JM.pdf (last visited July 7, 2022). It is "often worn by children" and "is designed to maintain a vertical, or neutral heel while also supporting the three arches of the foot. This can help improve standing, balance and walking." *Id.*

[18] Pronation is "the act of assuming the prone position, or the state of being prone. Applied to the hand, the act of turning the palm posteriorly (or inferiorly when the forearm is flexed), performed by medial rotation of the forearm. Eversion of the foot is sometimes referred to as pronation of the foot." *Dorland's* at 1526.

episode of myelopathy in 2015." *Id.* She recommended further testing and potentially a repeat MRI of M.P.'s spine. *Id.*

M.P. presented for her five-year well-child visit on May 14, 2019. *Id.* at 20–21. Petitioner reported that she still had concerns regarding M.P.'s speech. *Id.* at 20. She noted that "[s]ometimes [M.P.'s] words come out backwards in a sentence when speaking[and she f]orgets what some words are." *Id.* Petitioner indicated that M.P. was receiving a speech evaluation through her school. *Id.* M.P.'s examination was normal. *Id.* at 22–24. M.P.'s pediatrician recommended a follow-up in one year. *Id.* at 24. Petitioner has not filed any additional medical records.

B. Petitioner's Affidavit & Fact Testimony

Petitioner submitted one affidavit in support of her petition and testified at the entitlement hearing. *See* Pet'r's Ex. 33, ECF No. 57-1; Tr. 12–22. Petitioner's description of the onset of M.P.'s symptoms post vaccination was consistent with M.P.'s medical records. Pet'r's Ex. 33 ¶ 5. Petitioner testified that "prior to [M.P.] getting sick or being injured, she was like a normal one-year-old." Tr. 13:12–13. Petitioner wrote that M.P. "began to show signs of being sick on May 18, 2015, with a cough, fever, and congestion." Pet'r's Ex. 33 ¶ 5. On May 25, 2015, M.P.'s "fever was 102.6 [degrees Fahrenheit] and she suffered from vomiting and diarrhea." *Id.* ¶ 6. M.P. "was also crying and apparently in pain." *Id.* Petitioner attested that "M.P.'s condition kept deteriorating. She became very, very lethargic." *Id.* ¶ 7. She noted that M.P. "was sleeping much more than usual. When she awoke, she did not want to eat or drink[,] and she did not interact with [Petitioner] like she normally did." *Id.* Petitioner continued that M.P. "had a loss of balance and would fall backwards if not supported." *Id.* "She was[not] using her arms like she normally did and then she was unable to walk." *Id.* Petitioner testified that when M.P. lost the ability to walk, she also "could[not] roll over . . . [or] sit up." Tr. 13:16–18.

From there, Petitioner described M.P.'s initial hospitalization on May 27, 2015. Pet'r's Ex. 33 ¶ 8. She noted that M.P. "could[not] use her hands to hold her bottle." Tr. 13:19–20. Petitioner wrote that M.P. "spent [thirteen] days in the hospital and among [sic] numerous test[s] and procedures, [including] a lumbar puncture and an MRI[, . . . she] was diagnosed with [TM] and [ADEM]." Pet'r's Ex. 33 ¶¶ 8–9. Petitioner noted that M.P. needed PT to regain her ability to walk. *Id.* ¶¶ 10–11.

Petitioner explained the level of care M.P. received. Tr. 15:17–24. Petitioner explained that M.P.'s PT began while she was still in the hospital and continued in their home with a physical therapist for about two years. Tr. 14:3–18, 16:1–3. Petitioner stated that M.P. continues to receive PT at home with Petitioner by "walk[ing] around the block . . . walk[ing] on uneven surfaces, [and] walking backwards." Tr. 16:4–8. She noted that M.P. tells Petitioner that her legs or feet hurt following their walks or after a lot of activity. Tr. 17:5–8. Petitioner testified that she "would have to massage [M.P.'s] legs and her feet quite often." Tr. 17:8–9. She also described doing "little baby leg lifts" to "help strengthen [M.P.'s] abdominal muscles." Tr. 16:8–11. She noted that M.P. started off wearing AFOs for about a year "to help support her feet and walking." Tr. 15:20–23. "Later on, she was also fitted for orthotics for her shoes," which she wore for another year. Tr. 15:21–24.

Petitioner testified that at age three to four, M.P. was doing "okay." Tr. 16:24–25. She stated that M.P. attended pre-school but "would come home very tired, very fatigued." Tr. 17:1–

2. M.P. would also tell Petitioner that her legs hurt after "playground time on the slides and stuff[.]" Tr. 17:2–4. Petitioner testified that M.P. is in age-appropriate first grade and "has[not] had any issues of testing for a lower grade[.]" Tr. 19:1–3. However, "strenuous activity does [still] cause her pain afterwards." Tr. 17:11–14. A lot of strenuous activity, such as playing in the pool, Petitioner explained, causes M.P. to be "pretty tired[]" and to need naps. Tr. 17:14–19. Petitioner also noted that as a result of her speech delays, M.P. "still does tend to put words in the wrong order[]" and struggles "finding the right word to say." Tr. 18:5–24.

On cross-examination, Petitioner was asked about her eldest daughter's illness prior to the onset of M.P.'s symptoms. Tr. 19:17–25, 20:1–3. Petitioner testified that she did not recall her eldest daughter being sick with pneumonia around May 18, 2015, but Petitioner stated that if the medical records reflect that, she did not have a reason to doubt their accuracy. Tr. 20:4–15, 21:8–20. She also stated that she and her husband were both sick following M.P.'s hospitalization with "a cold[,]" but that they did not seek medical treatment. Tr. 20:16–23.

III. Experts

A. Expert Review

1. Petitioner's Expert, Lawrence Steinman, M.D.

Dr. Steinman received his medical degree from Harvard University in 1973. Pet'r's Ex. 20 at 1. He completed his post-graduate training at Stanford University, where he completed an internship in surgery in 1973, a residency in pediatrics in 1974, and a residency in pediatric and adult neurology from 1977 to 1980. *Id.* He became board certified in neurology in 1984. *Id.* at 2. He served as the Chairman of the Immunology Program at Stanford for approximately ten years from 2002 to 2011. *Id.* at 1. He currently serves as a professor of neurology, pediatrics, and genetics in Stanford University's Department of Neurology and Neurological Sciences. *Id.* Dr. Steinman's curriculum vitae includes over five-hundred and forty published articles of which he is a listed author. *See id.* at 5–45.

During the hearing, he noted that he also "did a fellowship in chemical immunology[, which is] the chemistry applied to immunology." Tr. 23:19–20. Dr. Steinman testified that he is currently a "general neurology attending, [and] also get[s] called in consultation . . . on cases where having some immunology background could assist the team." Tr. 24:6–9. He further noted that he runs a research laboratory, and his research is based in "trying to understand how the nervous system is attacked by the immune system[]" in diseases such as multiple sclerosis ("MS"). Tr. 24:11–15.

Dr. Steinman submitted two expert reports and testified during the entitlement hearing. *See* Pet'r's Exs. 19, 21; Tr. 22–101, 174–188. Petitioner "presented" Dr. Steinman "as an expert in neurology and immunology[]" without objection. Tr. 26:2–21.

2. Respondent's Expert, Hayley Gans, M.D.

Dr. Gans received her medical degree from the State University of New York Health Science Center at Syracuse in Syracuse, New York in 1991. Resp't's Ex. B at 1. Dr. Gans completed an internship and residency in pediatrics at Stanford University School of Medicine in

1992 and 1994, respectively. *Id.* She also completed a fellowship in pediatric infectious diseases from the same institution in 1998. *Id.* Dr. Gans served as an assistant professor of pediatrics at Stanford from 2006–2015. *Id.* She has been a clinical associate professor at the same institution since 2015. *Id.* Dr. Gans is board certified in pediatrics and pediatric infectious diseases. *Id.* She has received several honors and awards, has served on numerous committees, and holds memberships in several professional and scientific societies. *Id.* at 2–3. Her curriculum vitae lists nearly one hundred publications, including articles, abstracts, book chapters, and presentations of which she is a listed author. *See id.* at 4–7. The "bulk of [her] work has been on the immune response to vaccines." Tr. 142:8–9.

Discussing her clinical practice, Dr. Gans testified during the hearing that she "initially [] practiced in both pediatric infectious disease clinical service as well as serving in the immunology clinics at Stanford University in the pediatrics hospital." Tr. 138:17–20. She currently "codirect[s] the pediatric infectious disease committee for immunocompromised hosts." Tr. 138:25, 139:1. Dr. Gans also "serv[es] in the general pediatric infectious disease service at Stanford." Tr. 139:4–5. She testified that she treats patients and has "direct patient care responsibilities[]" but is a "consultant[] on the service." Tr. 139:6–11. Dr. Gans explained that she is "brought in" to care for individuals who have "any form of demyelination [including] . . . ADEM, [TM], other encephalitis, encephalopathy or other neurologic conditions." Tr. 139:15–20. She noted that part of the reason she is brought in is because "infections are a large part of the cause of these outcomes." Tr. 139:22–23. As part of her research, Dr. Gans "focuses on the host pathogen interface, so sort of the immune response to a[n] infection or pathogen, . . . using immunizations in children to actually look at their immune response." Tr. 140:1–7. Dr. Gans stated that she has testified twice in the Vaccine Program. Tr. 142:22–25, 143:1–4.

Dr. Gans submitted two expert reports and testified during the entitlement hearing. Resp't's Exs. A, E; Tr. 137–174. Respondent offered Dr. Gans as an expert in pediatrics, pediatric infectious diseases, and pediatric immunology specifically related to vaccinations without objection, and I recognized her as such. Tr. 143:15–25, 144:1–24.

3. Respondent's Expert, Michael Kruer, M.D.

Dr. Kruer received his medical degree from the University of Arizona College of Medicine in 2004. Resp't's Ex. D at 2. He completed a residency in pediatrics in 2007 at Phoenix Children's Hospital. *Id.* at 1–2. He also completed fellowships in molecular neurogenetics and neurodevelopmental disabilities at Oregon Health & Science University in 2011. *Id.* He is board certified in pediatrics, neurology, and neurodevelopmental disabilities. *Id.* at 1. Dr. Kruer previously served as an assistant professor of pediatrics and neurosciences at the University of South Dakota College of Medicine. *Id.* He also served as an attending neurologist and associate scientist at Sanford Children's Hospital in Sioux Falls, South Dakota. *Id.* He currently serves as an associate professor in the departments of Child Health, Cellular & Molecular Medicine and Neurology at the University of Arizona College of Medicine in Phoenix. *Id.* He is also the Director of the Pediatric Movement Disorders Program at Phoenix Children's Hospital. *Id.* Dr. Kruer serves on several boards and committees and has received numerous honors and awards. *Id.* at 2–5. His curriculum vitae includes approximately eighty publications of which he is a listed author. *See id.* at 5–25.

During the hearing, he noted he "did a fellowship in neuroimmunology." Tr. 103:13–14. Dr. Kruer explained that his specialization is in neurogenetics and neuroimmunology. Tr. 104:11–12. He stated that about forty percent of his time is spent seeing patients and the remaining time is "[s]pent conducting patient-oriented research and performing administrative and teaching duties." Tr. 104:13–17. Dr. Kruer testified that he treats patients with demyelinating conditions "quite often[.]" Tr. 104:18–23. He noted he has testified "over a dozen" times in the Program. Tr. 106:12.

Dr. Kruer submitted two expert reports and testified during the entitlement hearing. *See* Resp't's Exs. C, F; Tr. 102–136. Respondent offered Dr. Kruer as an expert in pediatric neurology and neuroimmunology. Tr. 106:13–15. Petitioner did not object to offering Dr. Kruer as an expert in pediatric neurology but noted an objection to his admission as an expert in immunology. Tr. 106:22–25, 107:1–16. Dr. Kruer then testified under voir dire that he is "a fellowship-trained clinical neuroimmunologist." Tr. 108:9–10. He has "published a number of papers in the field, [and he is] one of the attending physicians within the division of pediatric neuroimmunology at Phoenix Children's Hospital's Barrow Neurologic Institute." Tr. 108:11–15. Petitioner rescinded her objection and Dr. Kruer was admitted as an expert in pediatric neurology and immunology. Tr. 108:16–21.

B. Expert Reports and Testimony

1. Petitioner's Expert, Dr. Steinman

Dr. Steinman submitted two expert reports and testified during the hearing. *See* Pet'r's Exs. 19, 21; Tr. 22–101, 174–188. Dr. Steinman "100 percent" agreed with M.P.'s diagnoses of TM and ADEM. Pet'r's Ex. 19 at 4; Tr. 35:5–7. He defined ADEM as "the example of when the immune system attacks something in the brain." Tr. 38:20–21. He noted that "it extends both in experimental animal[models] and in humans often down into the spinal cord, so you get this involvement in both the brain and the spinal cord." Tr. 39:8–11. Dr. Steinman testified that there are many different manifestations of ADEM, including encephalopathy, alterations in the level of consciousness, motor and sensory problems, and issues with the autonomic nervous system. Tr. 39:12–18. Dr. Steinman defined TM as "a similar phenomenon where the immune system impacts structures in the spinal cord, leading to paralysis, sensory loss, [and] autonomic disorders." Tr. 39:24–25, 40:1. Dr. Steinman concluded that "[i]f not for the vaccines [M.P. received] on May 14, 2015, and the contemporaneous infection with the human metapneumovirus, she would not likely have developed neuroinflammation with acute [TM] and ADEM." Pet'r's Ex. 19 at 2.

Dr. Steinman wrote this occurrence was possible because of the concept of molecular mimicry. *Id.* at 6. He relied on an article he wrote containing a diagram, which "describes how shared structures on a virus or bacteria or in a vaccine can trigger a cross-reactive response to [it]self[,]" to demonstrate the concept. *Id.* (citing Pet'r's Ex. 55 at 4, ECF No. 75-1).[19] He noted in the article that "a foreign antigen may resemble antigen[s] produced by the body. Such molecular mimicry provokes the T cells to attack body tissues that contain the self-antigens." *See id.*

[19] L. Steinman, *Autoimmune Disease,* 269 SCIENTIFIC AMERICAN 106–14 (1993).

Dr. Steinman further explained the concept of molecular mimicry and supported his theory with studies on experimental autoimmune encephalomyelitis ("EAE"),[20] "to [help] understand how the components of the MMR and varicella vaccines and the human metapneumovirus might trigger neuroinflammation in the brain and the spinal cord of M.P." *Id.* at 5–6 (citing Pet'r's Exs. 50–53, ECF Nos. 74-6–74-9).[21] He noted that he relied on EAE as a comparison because "[t]he experimental model of ADEM involves transverse myelitis . . . and is known as [EAE]." *Id.* at 5. Dr. Steinman wrote that "the latest version of this EAE, acute optic neuritis[,] . . . provides a test system for investigating one of the most common clinical presentations of an adverse reaction to routine vaccination." *Id.* at 6 (citing Pet'r's Ex. 51).[22, 23] Dr. Steinman authored a commentary on EAE and explained that Dr. Thomas Rivers and his colleagues "established [the first model of EAE] to try to understand what caused neurological reactions to certain viral infections like smallpox and in some circumstances to vaccinations like rabies[.]" *See id.* Dr. Rivers found that following diseases such as smallpox, vaccinia and measles, and during or post rabies vaccination, "an occasional patient develops symptoms and signs referable to the central nervous system." *See* Pet'r's Ex. 51 at 1. Dr. Steinman indicated that "studies on the EAE model" bring together "seemingly opposite poles of immunity[,]" allergy and autoimmunity, because such studies show that "components of the allergic response are critical in the modulation of Th1 autoimmunity[]" to produce neuroinflammation. *Id.* Dr. Steinman also addressed the Absoud et al.[24] article filed by Respondent and noted that the authors determined that "molecular mimicry, . . . [is] one of the two proposed mechanisms" for spinal cord inflammation and the development of TM. Tr. 68:17–23 (citing Resp't's Ex. A, Tab 17 at 4, ECF No. 37-7).

Dr. Steinman then discussed the target of the molecular mimic in his theory. Pet'r's Ex. 19 at 5. He wrote that the body produces "adaptive immune responses to two key myelin antigens, myelin basic protein ("MBP") and myelin oligodendroglial glycoprotein ("MOG")[, which] are

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[20] Experimental autoimmune encephalomyelitis or experimental allergic encephalomyelitis ("EAE") is "an animal model for acute disseminated encephalomyelitis [ADEM,] in which the characteristic pathophysiology and clinical signs of this disease are produced by immunization of an animal with extracts of brain tissue or with myelin basic protein together with Freund adjuvant[.]" *Dorland's* at 614. EAE is an umbrella term for inflammatory demyelinating diseases, including optic neuritis and neuromyelitis optica. Dr. Steinman noted that since EAE's "first description . . . the model has served as a starting point for our understanding of autoimmunity[.]" Pet'r's Ex. 51 at 1. Dr. Steinman did not otherwise describe what he meant by the word "experimental."

[21] S. Sagan, et al., *Tolerance Checkpoint Bypass Permits Emergence of Pathogenic T cells to Neuromyelitis Optica Autoantigen Aquaporin-4,* 113(51) PROC. NAT'L ACAD. SCI. 14781–86 (2016); L. Steinman, *Optic Neuritis, A New Variant of Experimental Encephalomyelitis, A Durable Model for All Seasons, Now in its Seventieth Year,* 197:9 J. EXP. MED. 1065–72 (2003); A. Gautam, et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. EXP. MED. 605–09 (1992); A. Gautam, et al., *Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity,* 91 PROC. NAT'L ACAD. SCI. 767–71 (1994).

[22] L. Steinman, *Optic Neuritis, A New Variant of Experimental Encephalomyelitis, A Durable Model for All Seasons, Now in Its Seventieth Year,* 197:9 J. EXP. MED. 1065–72 (2003).

[23] Dr. Steinman cites to reference number 18 in his report as support for this argument, which corresponds to an article by Sagan et al. However, his discussion appears to actually quote reference number 19, an article authored by Dr. Steinman himself. I believe this error was inadvertent.

[24] M. Absoud, et al., *Pediatric Transverse Myelitis,* 87 NEUROL. 47–52 (2012).

detectable and likely critical in the pathogenesis of [TM] and ADEM." *Id.* Dr. Steinman relied on medical literature to support his opinion. He cited an article by Abramsky et al.,[25] which noted that MBP, "one of the major proteins of the myelin sheath, is one of the targets of the immune system" in TM. Tr. 54:20–25 (citing Pet'r's Ex. 45 at 3, ECF No. 74-1). Similarly, O'Connor et al.[26] found that another antigen targeted in ADEM is MOG. Tr. 55:2–6 (citing Pet'r's Ex. 46 at 2, ECF No. 74-2). The article by van Haren et al.[27] indicated that "autoantibodies to defend components of myelin in ADEM, . . . included MOG antibodies and [MBP] antibodies." Tr. 56:18–25 (citing Pet'r's Ex. 47, ECF No. 74-3). The authors of the Zamvil et al.[28] article noted that "one of the known antigenic targets of [TM] is MOG." Tr. 57:11–16 (citing Pet'r's Ex. 48 at 1, ECF No. 74-4). Dr. Steinman further relied on a case study by Rostasy et al.[29] showing a patient with neuromyelitis optica ("NMO"), a subset of acute demyelinating diseases, who tested negative for aquaporin-4 (the antigen relevant to NMO) but was positive for MOG antibodies. Tr. 57:22–25, 58:1–8 (citing Pet'r's Ex. 49 at 1–2, ECF No. 74-5). Dr. Steinman stated that this study described "findings that are somewhat similar to what was seen in M.P." Tr. 58:5–6. Dr. Steinman noted that M.P. was also negative for aquaporin-4 and was not tested for MOG antibodies. Tr. 58:2–3. He argued that this body of literature therefore supports his position that "MOG is high up on the list of what might be in the vaccine that is known to be associated with [ADEM and TM]." Tr. 58:6–8. He did not elaborate on this point but further used these articles to argue that "the mimics that [he] found . . . are relevant to the disease that[is] in question." Tr. 57:3–6.

Dr. Steinman addressed the fact that "immunity to nervous system antigens like myelin is rather widespread in" healthy individuals. Pet'r's Ex. 21 at 4, 6. He wrote that "[o]ne of the reasons that most normal individuals are free of autoimmune demyelinating disease is that immunity to myelin is necessary but not sufficient to get actual disease." *Id.* at 6. To get actual disease and a self-reactive immune response to peripheral nerves triggering ADEM and TM, "[o]ther genetic and environmental factors are necessary[.]" *Id.* He cited an article by Ota et al.,[30] which showed that "there are T cells reactive to [MBP]" in healthy individuals. *Id.* at 4 (citing Pet'r's Ex. 58 at 2, ECF No. 75-4). He also cited an article by Pette et al.,[31] demonstrating that "in healthy individuals[,] T cells reactive to [MBP] were as readily detectable as in [multiple sclerosis] patients[.]" *Id.* at 5 (citing Pet'r's Ex. 59 at 1, 3, ECF No. 75-5). Dr. Steinman relied on the Ota et al. and Pette et al. studies to demonstrate that "you can detect immune responses in healthy people without multiple sclerosis [in] the [MBP,]" which is also "one of the antigens . . . target[ed] in

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[25] O. Abramsky & D. Teitelbaum, *The Autoimmune Features of Acute Transverse Myelopathy,* 2 ANN. NEUROL. 36–40 (1977).

[26] K. O'Connor, et al., *Self-antigen tetramers discriminate between myelin autoantibodies to native or denatured protein,* 13(2) NAT. MED. 211–17 (2007).

[27] K. van Haren, et al., *Serum autoantibodies to myelin peptides distinguish acute disseminated encephalomyelitis from relapsing-remitting multiple sclerosis,* 19 MULT. SCLER. 1–10 (2013).

[28] S. Zamvil & A. Slavin, *Does MOG Ig-positive AQP4-seronegative opticospinal inflammatory disease justify a diagnosis of NMO spectrum disorder?,* 2:62 NEUROL. NEUROIMMUNOL. NEUROINFLAMM. 1–7 (2015).

[29] K. Rostasy, et al., *Persisting myelin oligodendrocyte glycoprotein antibodies in aquaporin-4 antibody negative pediatric neuromyelitis optica,* 19(8) MULT. SCLER. 1052–59 (2012).

[30] K. Ota, et al., *T-Cell Recognition of an Immuno-Dominant Myelin Basic Protein Epitope in Multiple Sclerosis,* 346 NATURE 183–88 (1990).

[31] M. Pette, et al., *Myelin Basic Protein-Specific T Lymphocyte Lines from MS Patients and Healthy Individuals,* 40 NEUROL. 1770–78 (1990).

[TM].” Tr. 64:8–14, 65:7–11 (citing Pet’r’s Exs. 58–59). Dr. Steinman stated that the authors of these studies found that “even though it[is] necessary to have these types of responses, it[is] not sufficient, because you can have that response, and there are certain features in those individuals which make them continue to be healthy despite easily being able to detect such responses.” Tr. 64:18–23. He referred to this as the concept of a “host response.” Tr. 65:4–6. Dr. Steinman maintained that “molecular mimicry is a key mechanism in understanding how tolerance to ‘self’ structures like myelin proteins is broken.” Pet’r’s Ex. 21 at 6.

As further support for his theory, Dr. Steinman ran numerous “BLAST” searches using the protein database compiled by the National Library of Medicine to identify homologies between the components of the MMR and varicella vaccines and the human metapneumovirus “to see if there were any homologies with either [MBP] or with [MOG]” as they are the two proteins known to be “under scrutiny” in ADEM and TM. Pet’r’s Ex. 19 at 7; Tr. 55:10–19. Dr. Steinman “explicit[ly]” noted that he “found [homology] in each component of the two vaccines [M.P. received], but [] also found it in the metapneumovirus.” Tr. 55:23–25, 60:25–61:1. Based on these findings, Dr. Steinman maintained that all three factors worked in concert to cause M.P.’s TM and ADEM. Tr. 56:1–9. Dr. Steinman opined that the combination of the MMR and varicella vaccinations with M.P.’s human metapneumovirus “created a ‘perfect storm’ whereby the three components . . . all contain molecular mimics with key myelin proteins, known to be targeted in acute [TM] and ADEM[,]” which caused her injuries. Pet’r’s Ex. 19 at 1–2. He noted that in all cases where he finds homology of a relevant protein or enzyme to the disease, he could make an argument that there could be causation. Tr. 98:16–21. But in cases where he finds homology but is unable to find it to a relevant enzyme, “he would[not] participate in the case.” Tr. 100:22–101:5. Overall, “homology is not enough for [him].” Tr. 101:8–9. He requires the homology to “be in one of the proteins or enzymes that[is] implicated in the disease.” Tr. 101:9–11.

Prior to discussing his specific findings of the BLAST searches, Dr. Steinman relied on medical literature to support his “criterion for a ‘meaningful molecular mimic[.]’” Pet’r’s Ex. 19 at 7 (citing Pet’r’s Exs. 51–54);[32] *see also* Tr. 58:15–20. Dr. Steinman[33] asserted that these articles showed that the “identity of 5 of 12 amino acids, not even consecutive amino acids, was sufficient to trigger experimental encephalomyelitis[]” in animal models. *See id.* He argued that an article by Gautam et al.[34] showed that 5 of 11 amino acids were identical between a herpesvirus and MBP, with only 3 consecutive proteins but the authors “were [still] able to induce encephalomyelitis” in mice. Pet’r’s Ex. 19 at 8 (citing Pet’r’s Ex. 54 at 1, 5). Dr. Steinman further argued that a second

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[32] L. Steinman, *Optic Neuritis, A New Variant of Experimental Encephalomyelitis, A Durable Model for All Seasons, Now in its Seventieth Year,* 197:9 J. EXP. MED. 1065–72 (2003); A. Gautam, et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. EXP. MED. 605–09 (1992); A. Gautam, et al., *Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity,* 91 PROC. NAT’L ACAD. SCI. 767–71 (1994); A. Gautam, et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis,* 161 J. IMMUNOL. 60–64 (1998).

[33] It appears that Dr. Steinman cited incorrect reference numbers within his expert report and that such cites to references 19–22 are off by one number. *See* Pet’r’s Ex. 19. I believe this error was inadvertent, and I will cite to each reference based on the correct article.

[34] A. Gautam, et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis,* 161 J. IMMUNOL. 60–64 (1998).

article by Gautam et al.[35] showed that "identity at 5 amino acids" in a chain of 6 peptides was sufficient to trigger neuroinflammation in mice. *Id.* at 8–9 (citing Pet'r's Ex. 53 at 1, 4). He cited a third article by Gautam et al.[36] to show that "a peptide with 4 of 11 amino acids induced neuroinflammation[]" in mice. *Id.* at 9–10 (citing Pet'r's Ex. 52 at 2–3). Dr. Steinman summarized overall that the "criterion [sic] [described in the medical literature] was sufficient to provide experimental evidence for eliciting experimental ADEM when such mimics were injected into mice." Pet'r's Ex. 21 at 2. Dr. Steinman acknowledged that having 12 out of 12 identical amino acids would have "a higher incidence and a stronger disease[,]" but he maintained that 5 out of 12 was a minimum sequence. Tr. 58:20–21, 60:9–17 (citing Pet'r's Exs. 52–54). He noted that he "put the line in the sand at [a sequence of] 5 out of 12[]" amino acids. Tr. 60:20–24.

Dr. Steinman then discussed the results from his eleven "BLAST" searches targeted at MOG or MBP versus the components of the MMR and varicella vaccines and the HMPV infection. *See* Pet'r's Ex. 19 at 6–28; *see also* Pet'r's Exs. 42–43, ECF Nos. 73-8–73-9.[37] Dr. Steinman did not discuss findings associated with the human metapneumovirus versus MBP. *See* Pet'r's Ex. 19 at 28. Of his eleven BLAST searches, seven revealed homologies of at least 5 out of 12 identical amino acids for a statistically significant match susceptible to molecular mimicry consistent with the literature. *Id.* at 6–28; Pet'r's Exs. 52–54.[38] Dr. Steinman argued that all matches from his eleven BLAST searches reached the threshold for inducing neuroinflammation sufficient to cause experimental ADEM described in the medical literature. *See id.* He testified that his theory of molecular mimicry does not change depending on whether the vaccine contained a live virus or not. Tr. 75:8–18.

Dr. Steinman addressed Dr. Kruer's discussion that one of the Gautam et al.[39] articles showed mimics with many plant viruses, including shallot and cabbage leaf curl viruses, and MBP. Pet'r's Ex. 21 at 3 (citing Pet'r's Ex. 54 at 3). Dr. Steinman opined that "finding such homologies is not unexpected." *Id.* Paying close attention to green beans, Dr. Steinman found a study discussing such a finding. *Id.* at 4. He relied on the Daroca et al.[40] article wherein three patients developed asthma and rhinitis "caused by exposure to raw, but not to cooked, green beans[]" via molecular mimicry. *Id.* (citing Pet'r's Ex. 57 at 1, ECF No. 75-3). All patients "tolerated [the]

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[35] A. Gautam, et al., *Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity,* 91 PROC. NATL. ACAD. SCI. 767–71 (1994).

[36] A. Gautam, et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. EXP. MED. 605–09 (1992).

[37] *MMR II (Measles-Mumps-Rubella Virus Vaccine Live) – Package Insert,* FOOD & DRUG ADMINISTRATION (https://www.fda.gov/vaccines/MMRII); *Varivax Varicella Virus Vaccine Live – Package Insert,* FOOD & DRUG ADMINISTRATION (https://www.fda.gov/vaccines/varivax).

[38] A. Gautam, et al., *A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,* 176 J. EXP. MED. 605–09 (1992); A. Gautam, et al., *Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity,* 91 PROC. NAT'L ACAD. SCI. 767–71 (1994); A. Gautam, et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Signs of Experimental Autoimmune Encephalomyelitis,* 161 J. IMMUNOL. 60–64 (1998).

[39] A. Gautam, et al., *supra* note 34.

[40] P. Daroca, et al., *Asthma and Rhinitis Induced by Exposure to Raw Green Beans and Chards,* 85 ANN. ALLERGY ASTHMA IMMUNOL. 215–18 (2000).

ingestion of green beans." *Id.* He noted that the authors found that "the route of administration and the route of exposure is exceptionally important." Tr. 92:19–25 (citing Pet'r's Ex. 57). The patients in the study who experienced a reaction to raw green beans did not have a reaction when they ingested the same. *See* Pet'r's Ex. 57. Dr. Steinman summarized that oral challenges in the Daroca et al. study were negative, "but exposure to other routes was allergenic." Pet'r's Ex. 21 at 4. Dr. Steinman opined that the "route of introduction of a molecular mimic is quite critical to whether or not it would be capable of inducing ADEM or TM." *Id.* Dr. Steinman alluded to the fact that vaccines are injected and posited, "[i]f we injected green beans [into oneself], [he] wonder[s] what would happen." *Id.*; Tr. 93:1–3.

Dr. Steinman relied on additional medical literature to support his theory that the MMR and varicella vaccines can trigger ADEM and TM and did so in M.P.'s case. An article by Bennetto and Scolding[41] noted that the MMR vaccine is associated with ADEM. Pet'r's Ex. 19 at 4 (citing Pet'r's Ex. 41 at 2–3, ECF No. 73-7); Tr. 43:17–25, 44:1–3. The authors found that "the non-neural measles, mumps, and rubella vaccinations are most commonly associated with post-vaccination encephalomyelitis." *See* Pet'r's Ex. 41. He also relied on the article by Young et al.,[42] which indicated that "[n]umerous infections, mostly viral, and other immunologic triggers such as vaccinations have been associated with ADEM[.]" Tr. 40:20–22 (citing Pet'r's Ex. 28 at 3, ECF No. 56-3). The information published by Boston Children's Hospital[43] noted that "ADEM may [] follow a vaccination, although this is rare." Tr. 41:20–24 (citing Pet'r's Ex. 31 at 2, ECF No. 56-6). He further relied on the National Institute of Health's ADEM information page, which noted that "ADEM often follows viral or bacterial infections, or less often, vaccination for measles, mumps, or rubella." Tr. 40:25, 41:1–9 (citing Pet'r's Ex. 29, ECF No. 56-4).[44] Dr. Steinman argued this description is "highly pertinent" to M.P.'s case because she had a metapneumovirus and a vaccination with MMR. Tr. 41:9–11. Dr. Steinman cited an abstract by Stuve et al.[45] showing that ADEM's "clinical symptoms follow an infection or vaccination." Tr. 45:22–25, 46:11–19 (citing Pet'r's Ex. 27, ECF No. 56-2). He testified that the authors of the Klein et al.[46] article filed by Respondent found that there were "seven outcomes based on being known adverse outcomes, . . . theoretical/biologically plausible outcomes following MMR and/or varicella vaccines, ADEM, ataxia, arthritis, encephalitis, meningitis, encephalopathy, and [] Kawasaki" disease. Tr. 70:10–15 (citing Resp't's Ex. C, Tab 6 at 3, ECF No. 41-6). However, on cross-examination, Dr. Steinman admitted that the study did not contain data showing increased incidents of disease or "signal" after vaccinations. Tr. 83:2–5 (citing Resp't's Ex. C, Tab 6).

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[41] L. Bennetto & N. Scolding, *Inflammatory/Post-Infectious Encephalomyelitis,* 75 J. NEUROL. NEUROSURG. PSYCH. 22–28 (2004).

[42] N.P. Young, et al., *Acute Disseminated Encephalomyelitis: Current Understanding and Controversies,* 28:1 SEMIN. NEUROL. 84–94 (2008).

[43] *Acute Disseminated Encephalomyelitis (ADEM) – Symptoms & Causes,* BOSTON CHILDREN'S HOSPITAL (http://www.childrenshospital.org/conditions-and-treatements/conditions/a/acute-disseminated-encephalomyelitis-adem/symptoms-and-causes).

[44] *Acute Disseminated Encephalomyelitis Information Page,* NAT'L INST. OF NEUROL. DISORDERS & STROKE (https://www.ninds.nih.gov/Disorders/All-Disorders/Acute-Disseminated-Encephalomyelitis-Information-Page).

[45] Abstract of O. Stuve, et al., *Acute disseminated encephalomyelitis. Pathogenesis, diagnosis, treatment, and prognosis,* 76(6) NERVENARZT 701–07 (2005).

[46] N. Klein, et al., *Safety of Measles-Containing Vaccines in 1-Year-Old Children,* 135:2 PEDIATR. 322–31 (2015).

On cross-examination, Dr. Steinman addressed the Baxter et al.[47] article, which found that there was no statistically significant increased risk of immunization in either the 5 to 28-day or the 2 to 42-day risk interval prior to the onset of TM. Tr. 83:12–14 (citing Resp't's Ex. E, Tab 1, ECF No. 50-2). The authors also found that the Tdap vaccine was associated with a statistically significant increase in the risk in the 5 to 28-day exposure interval, but not the 2 to 42-day interval, for the onset of ADEM. Resp't's Ex. E, Tab 1. Dr. Steinman opined that the Baxter et al. study did not show data of increased incidents of disease or "signal" after vaccinations. Tr. 83:12–14. Dr. Steinman argued, however, that "the methodology [used in that study] would not allow a case like [M.P.'s] to even be addressed, because it dealt with only one vaccine at a time . . . so [the authors] would[not] have counted [M.P.'s] case." Tr. 83:15–17, 84:1.

On rebuttal, after much discussion regarding the wording used in the Baxter et al. study ("combination vaccines" versus "combinations of vaccines"), Dr. Steinman maintained that the authors purported not to "analyze combinations of vaccines[,]" so M.P.'s case would not have been captured by this study. Tr. 175:5–14 (citing Resp't's Ex. E, Tab 1). Despite the authors' inclusion of the sentence "we evaluated all administered vaccines, both individually and combined[,]" Dr. Steinman maintained that the authors analyzed vaccines with multiple viruses contained in the same syringe, such as the DTaP or MMR vaccines, rather than those requiring "two jabs[.]" Tr. 184:8–25, 185:1–10. Under my questioning, he read verbatim from the article which indicated the authors "did not analyze combinations of vaccines." Tr. 188:15–16 (citing Resp't's Ex. E, Tab 1).

Dr. Steinman also discussed literature showing an association with HMPV and ADEM. Dr. Steinman cited an article by Athauda et al.,[48] which found that the human metapneumovirus has been associated with ADEM "in a case where there was also an H1N1 influenza infection." Pet'r's Ex. 19 at 5 (citing Pet'r's Ex. 44 at 1, ECF No. 73-10). Dr. Steinman stated that the case report shows an instance of "multiphasic ADEM associated with both human metapneumovirus and influenza type A and H1N1." Tr. 44:15–25, 45:1 (citing Pet'r's Ex. 44). The patient in the study had not received any recent immunizations. Pet'r's Ex. 44 at 1. Dr. Steinman opined that this example "does[not] fit [M.P.'s case] perfectly, but it[is] certainly an example of the metapneumovirus [] caus[ing] ADEM." Tr. 45:10–13.

He then discussed the package inserts for the vaccines at issue. The MMR vaccine package insert notes an association with ADEM and TM. Pet'r's Ex. 19 at 4 (citing Pet'r's Ex. 42 at 7).[49] The package insert indicates that "[e]ncephalitis and encephalopathy have been reported approximately once for every 3 million doses of [the] MMR II or [MMR]-containing vaccine administered since licensure of these vaccines." *See id.* He testified that the package insert also "list[s] encephalitis, . . . encephalopathies, measles inclusion body encephalitis, . . . [ADEM], [TM], and so on[]" as "known adverse reaction[s] to [the] MMR vaccine." Tr. 42:10–24 (citing Pet'r's Ex. 42 at 7). He further relied on the package insert for the varicella vaccine to note that it

[47] R. Baxter, et al., *Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis,* 63:11 CLIN. INFECT. DIS. 1456–62 (2016).
[48] D. Athauda, et al., *Multiphasic Acute Disseminated Encephalomyelitis (ADEM) Following Influenza Type A (Swine Specific H1N1),* 259 J. NEUROL. 775–78 (2012).
[49] *See supra* note 37.

has been associated with encephalitis and TM. Pet'r's Ex. 19 at 4 (citing Pet'r's Ex. 43 at 5)[50]; Tr. 43:2–15.

Dr. Steinman argued that based on all the mimics found in his BLAST searches, and because ADEM and TM can be attributed to the MMR and varicella vaccines and to the human metapneumovirus infection, the "vaccinations and the infection constitute a 'perfect storm' for ADEM and TM" in M.P. Pet'r's Ex. 19 at 28. Dr. Steinman testified that the term "perfect storm" is "a metaphor . . . for many factors [that] caused the boat to go down[.]" Tr. 80:2–4. Specifically, he argued that the vaccines M.P. received on May 14, 2015, were a substantial factor in causing her injuries. Tr. 38:4–8, 74:18–21. As support for his theory that M.P.'s vaccines triggered mimics resulting in neuroinflammation and subsequent ADEM and TM, he reiterated that the mimics are present "in all potential factors[]" for M.P.'s condition. Tr. 76:12–14. Dr. Steinman explained that while "the presence of mimicry is necessary to explain how a vaccine or virus might cause [M.P.'s] diseases," the act of "simply having the [molecular] mimic would not be sufficient to get an autoimmune disease." Tr. 61:17–18. He opined that "[t]he host, in this case M.P., had to have some other things in her either genetics or from an environmental impact on her immune system that contributed to why she got sick." Tr. 61:18–21. Dr. Steinman argued that the other factor was her metapneumovirus. Tr. 45:16–17.

He relied on M.P.'s May 30, 2015 brain and spinal cord MRI findings, which showed evidence "consistent with [ADEM]" to show neuroinflammation. Tr. 31:23–25, 32:5–12, 33:5–7 (citing Pet'r's Ex. 5 at 162–64). He reiterated that the MRI showed "a long segment of the spinal cord with abnormalities, all the way from where the spinal cord becomes the brain stem to thoracic level 10, . . . and vague cord enhancement." Tr. 32:6–10. He further noted that there was "bilateral symmetrical periventricular T2 hyperintensities, and a subtle area of the so-called T2 hyperintensity[,] and T1 hypointensity in a brain structure called the corpus collosum." Tr. 33:2–5. Dr. Steinman testified that the MRI impression was consistent with neuroinflammation in the form of ADEM. Tr. 32:5–6. Dr. Steinman also noted that the MRI showed spinal cord abnormalities "that are a manifestation of extensive [TM]." Tr. 33:8–10. M.P.'s "neurologic exam was concerning for [] longitudinally extensive [TM]." Tr. 32:11–12. He further relied on M.P.'s abnormal CSF results and noted they were consistent with a manifestation of extensive TM. Tr. 33:8–11 (citing Pet'r's Ex. 5 at 163). Dr. Steinman explained that M.P.'s treaters "did a panel for multiple sclerosis, looking for IgG." Tr. 33:10–12 (citing Pet'r's Ex. 5 at 163). He testified that this is "not really a panel for multiple sclerosis. It [is] a panel for neuroinflammation, but that[is] the way [her treaters] reported it." Tr. 33:12–14. Dr. Steinman opined that M.P.'s treaters "were comprehensive." Tr. 33:15.

Dr. Steinman responded to Drs. Gans' and Kruer's expert reports, in which they opined that M.P.'s injuries could be explained by her human metapneumovirus alone. Pet'r's Ex. 21 at 1. Dr. Steinman pointed out that he "clearly stated" in his previous report that M.P. had an HMPV infection. *Id.* He acknowledged that HMPV alone can cause ADEM and TM. Tr. 81:2–4. He wrote that given the timeline of M.P.'s cold symptoms, including a runny nose beginning three days after her May 14, 2015 vaccinations, this was "most likely[] the onset of her HMPV symptoms." Pet'r's Ex. 21 at 1. Dr. Steinman opined that M.P.'s vomiting and loss of mobility reported on May 25 and 26, 2015, were the first symptoms of her ADEM with TM. *Id.* He posited that "[b]y that time,

[50] *See id.*

[M.P. was] at the time when the MMR and [v]aricella vaccines are most likely to cause the ADEM with TM." *Id.* He continued that based on his nearly 40 years of research and experience, "[t]here is no way for medical science, as it presently exists, to assign a percentage of cause from the three known potential choices[]" of M.P.'s injury. *Id.*; Tr. 62:16–18. He testified that there is not a known medical way to "parse out whether [M.P.'s] neurologic injury was caused by the varicella vaccine versus the metapneumovirus or the MMR or any of the components of the MMR vaccine[.]" Tr. 76:2–8. Dr. Steinman acknowledged that Dr. Gans did not attempt to assign a statistical percentage for the causes of M.P.'s ADEM and TM, rather she "state[d] that the HMPV is the 'more likely' cause." Pet'r's Ex. 21 at 1. Dr. Steinman opined that "[t]he term 'more likely' . . . assigns a percentage of greater than 50%, which is of course statistical and quantitative." *Id.* at 1–2.

He further highlighted that Dr. Gans did not provide any proof that "HMPV has been shown to be a more common identifiable cause of ADEM than MMR or [v]aricella vaccines." *Id.* at 2. Dr. Steinman stated that Dr. Gans merely opined that "viruses are a more common cause than vaccines." *Id.* Dr. Steinman argued that "Respondent cannot escape th[e] reality[]" that "we have three potential causes including the contents of the vaccines [M.P.] received." *Id.* He continued that M.P. did not experience her ADEM and TM until she was exposed to all three potential causes. *Id.* Under my questioning, Dr. Steinman testified that he would not have expected the course of M.P.'s illness to be different depending on whether it was caused by an infection versus vaccination. Tr. 96:8–12.

Dr. Steinman attacked Dr. Gans' position that M.P.'s family members showed signs of illness with HMPV around the same time as M.P. and therefore her vaccinations were not responsible for her injuries. Pet'r's Ex. 21 at 2; Tr. 36:4–10. Dr. Steinman interpreted M.P.'s older sister's May 21, 2015 pneumonia diagnosis and her parents' upper respiratory symptoms to mean that "everyone was infected with the same microbe[.]" Tr. 36:15–18. He opined that given M.P.'s positive testing for the metapneumovirus on May 28, 2015, "everyone had a pneumovirus infection." Tr. 35:9–19, 36:18–20 (citing Pet'r's Ex. 5 at 199). Dr. Steinman argued he "turn[ed] Dr. Gans' argument on its head," and highlighted that "none of [M.P.'s family members] got ADEM and TM, because they did not also have the MMR and [v]aricella vaccines." Pet'r's Ex. 21 at 2. Dr. Steinman stated that "[o]nly one person got vaccinated, and that person[, M.P.,] got [TM] and [ADEM]." Tr. 36:21–23, 56:11–15. Dr. Steinman maintained that this "fact reinforces Petitioner's case and emphasizes [his] line of reasoning[.]" *Id.* On cross-examination, to account for the different outcomes of the HMPV infection experienced by M.P. compared to her parents, Dr. Steinman agreed that there are differences in the immune system of someone M.P.'s age and someone her parents' ages. Tr. 85:16–17. He stated it is possible that an adult "could have had an infection in the past and built up a resistance or antibodies to an infection that a child may not have[.]" Tr. 85:18–22.

On rebuttal, Dr. Steinman responded to Dr. Gans' assertions that M.P. suffered a primary exposure to HMPV, versus her family members who experienced a secondary exposure, which is why M.P. developed ADEM and TM. Tr. 176:5–8. He opined it was speculation to assume "who had how many exposures to this virus and when they had them." Tr. 176:11–14. Furthermore, Dr. Steinman maintained that a "stronger argument" exists for the fact that "immunological reactions are much stronger in a secondary response[] because your immune system[is] all fired up[]"

because "[y]our antibodies [have a] much higher affinity. Your T-cells have memory." Tr. 176:18–22, 181:14–15. Dr. Steinman agreed that he and Dr. Gans are in a fundamental disagreement about the effect of multiple exposures to the same pathogen on the immune system. Tr. 180:20–25, 181:1–15. He maintained that based on this discussion, he was not "adding a component of rechallenge" to his theory of causation because he did not want to speculate about M.P.'s "first exposure or second exposure." Tr. 182:5–19.

Regarding timing, Dr. Steinman identified the onset of M.P.'s symptoms as occurring approximately eleven days post vaccination. Tr. 38:1. As support for this conclusion, he noted that the first sign of a neurological complaint occurred on May 27, 2015, when M.P. "was very weak and refusing to walk." Tr. 31:17–21. He further noted M.P. exhibited floppiness and was lethargic. Tr. 31:21. While Dr. Steinman noted that vomiting could be a sign of some neurological illnesses, including TM, he maintained that M.P.'s treaters did not note signs of neurological deficits until May 27, 2015. Tr. 28:19–25, 29:6–9 (citing Pet'r's Ex. 4 at 80–82). Dr. Steinman supported this position by noting that the visit note from May 25, 2015, indicates that M.P.'s neurologic examination showed she had a normal level of consciousness, normal motor and sensation, and "grossly normal" cranial nerves. Tr. 30:19–24 (citing Pet'r's Ex. 4 at 65). He testified, consistent with M.P.'s medical record, that her fever, vomiting, and diarrhea ceased around May 26, 2015, prior to the start of her neurologic symptoms. Tr. 31:3–12 (citing Pet'r's Ex. 4 at 77).

Dr. Steinman opined that the timing of the onset of M.P.'s symptoms after receipt of the vaccines was "appropriate to implicate the vaccine as causative[.]" Tr. 37:21–25, 73:2–5. Dr. Steinman argued that M.P.'s hospitalization and ADEM diagnosis within two weeks of her vaccinations "fits with [the] Bennetto and Scolding[]" article. Pet'r's Ex. 19 at 28 (citing Pet'r's Ex. 41).[51] The authors found the "[t]he timing of the first symptoms varies slightly with the precipitant: typically 1–14 days after non-neural vaccines, a week or less after the appearance of a rash in exanthematous [sic] illnesses, and 1–3 weeks (or more) after rabies inoculation." *See id.* He relied on the ADEM information page published by the Cleveland Clinic which noted that although rare, "on occasion ADEM occurs after a vaccination" but that "[m]ost cases of ADEM begin about seven to 14 days after the infection." Tr. 71:21–23, 72:2–6 (citing Pet'r's Ex. 30, ECF No. 56-5).[52] An article by Sapuan et al.[53] indicated that ADEM "occurs a few days to several weeks after infections or vaccinations." Tr. 72:19–20 (citing Pet'r's Ex. 32 at 1, ECF No. 56-7). He maintained that the onset of M.P.'s neurologic symptoms fits "[v]ery comfortably[]" within the appropriate onset timeframe described in the medical literature. Tr. 72:10–13.

2. Respondent's Expert, Dr. Gans

Dr. Gans submitted two expert reports and testified at the entitlement hearing. *See* Resp't's Exs. A, E; Tr. 137–174. She agreed that M.P. suffered from ADEM and TM. Tr. 145:23–25. Dr. Gans opined that the cause of M.P.'s ADEM and TM was her HMPV infection. Resp't's Ex. A at 7.

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[51] *See* L. Bennetto & N. Scolding, *supra* note 41.

[52] *Acute Disseminated Encephalomyelitis (ADEM),* CLEVELAND CLIN. (https://my.clevelandclinic.org/health/diseases/14266-acute-disseminated-encephalomyelitis-adem).

[53] S. Sapuan & H. Basri, *Acute Disseminated Encephalomyelitis (ADEM) Presenting with Bilateral Optic Neuritis,* 14(1) MALAYS. J. MED. SCI. 71–74 (2007).

Dr. Gans discussed M.P.'s medical records and noted that M.P.'s platelet count during her May 27, 2015 hospitalization was elevated, "suggesting inflammation[.]" *Id.* at 3 (citing Pet'r's Ex. 5 at 9). She noted that M.P.'s fever, rash, URI, otitis media, and anorexia are "all consistent with what has been described in young children who [] acquire their primary [] infection with HMPV[.]" *Id.* at 5. Dr. Gans opined that M.P.'s history "is entirely consistent with an infection caused by HMPV from the 10 days of intermittent fever and rash, URI symptoms, OM, AGE, refusal to eat, followed by progressive neurologic symptoms consistent with a spectrum of demyelinating disease." *Id.* at 6. She testified that HMPV can cause neurologic diseases and that she does not "believe that there[is] evidence to suggest [the MMR and varicella] vaccines caused [ADEM or TM] in this case[.]" Tr. 148:6–8, 149:1–6, 150:4–9 (citing Pet'r's Ex. 44).[54] Dr. Gans stated that M.P. "very clearly [] had an infection . . . [and w]e know very clearly that [] infection in itself solely as [a] cause of illness" with a "neurologic outcome, particularly ADEM and any form of that." Tr. 150:11–17. She therefore concluded that M.P.'s "clinical disease, work-up[,] and physicians' assessments of [her] condition support the presence of an acute illness with HMPV[,] which then progressed to demyelination." Resp't's Ex. A at 5.

As support for her assertion that HMPV was the "acute process" for M.P.'s injuries, Dr. Gans relied on M.P.'s family's illness around the same time as M.P. and her vaccinations. *Id.* at 5–6. Dr. Gans opined that M.P.'s family's illness was "most likely also HMPV," which circulates during the spring. *Id.* at 5. She noted that the neurologic outcomes of HMPV "are almost exclusively seen in children <3 years of age . . . [as] age is the major risk factor for severe disease secondary to HMPV." Resp't's Ex. E at 2 (citing Resp't's Exs. A, Tabs 1–5, ECF Nos. 36-1–36-5).[55] Dr. Gans addressed Dr. Steinman's claim that while M.P.'s family members experienced illness around the same time as M.P., they did not develop neurologic symptoms because they did not also receive the vaccinations at issue. *Id.*; Tr. 158:3–5. Dr. Gans wrote that this assertion "is wrong." Resp't's Ex. E at 2. She explained that she does not "think that what you saw for M.P. was related to something in her immune system trigger[ing] her that then made her respond to the human metapneumovirus differently than the rest of her family." Tr. 169:16–19. She explained that "[r]ather, the reason why is because children are naïve to infections and upon first exposure experience more severe disease and more disseminated forms of the disease." Resp't's Ex. E at 2. Dr. Gans opined that M.P.'s May 2015 HMPV infection was her primary infection "given her age and the severity of her response." Tr. 158:15–16, 168:7–10, 172:3–6, 173:13–15. Dr. Gans stated that there is "variability" in the way people react to any pathogen. Tr. 158:7–8. She testified that "likely this was not the family's first interaction with this virus, and therefore, they[were] going to have a different immune response." Tr. 158:20–23. Dr. Gans testified that she thinks "the rest of her family had the advantage of having experienced this at a time when . . . their immune system was just going to allow them to handle it." Tr. 169:19–22. She therefore maintained that "age, not

[54] *See* D. Athauda, et al., *supra* note 48.

[55] B. van den Hoogen, et al., *A Newly Discovered Human Pneumovirus Isolated from Young Children with Respiratory Tract Disease,* 7:6 NATURE MED. 719–26 (2001); J. Kahn, *Epidemiology of Human Metapneumovirus,* 19:3 CLIN. MICROBIOL. REV. 546–57 (2006); V. Schildgen, et al., *Human Metapneumovirus: Lessons Learned over the First Decade,* 24:4 CLIN. MICROBIOL. REV. 734–54 (2011); J. Williams, et al., *Population-Based Incidence of Human Metapneumovirus Infection Among Hospitalized Children,* 201:12 J. INFECT. DIS. 1890–98 (2010); K. Edwards, et al., *Burden of Human Metapneumovirus Infection in Young Children,* 368:7 N. ENGL. J. MED. 633–44 (2013).

vaccine receipt, was the reason M.P. had [a] more severe disease than other family members with the same infection." Resp't's Ex. E at 2.

However, after much discussion, Dr. Gans stated that M.P. could still have developed ADEM after her secondary exposure to HMPV and that she is likely to have a severe reaction to HMPV anytime she is exposed. Tr. 172:10–22. Dr. Gans explained that the "immune response is going to be triggered in the same direction typically, no matter how many times [the patient] is exposed." Tr. 171:2–4. But because of cellular memory, the immune system "learn[s], and it[is] less severe the next time." Tr. 171:4–5.

She admitted that much of the pathophysiology about HMPV is unknown, but "appears highly associated with CNS manifestations that include demyelinating disease." Resp't's Ex. A at 6. As support, Dr. Gans relied on medical literature showing that an antecedent acute viral illness has been shown to be the cause of demyelinating processes more frequently than vaccines. *Id.* at 7. She cited several articles showing that the HMPV infection has been found to be the "second leading cause of bronchiolitis and pneumonia in children <5 years of age, with outbreaks peaking mostly during spring." *Id.* at 5 (citing Resp't's Exs. A, Tabs 1–5).[56]

Dr. Gans wrote that "[s]tudies have associated HMPV with acute encephalopathies ranging from subcortical encephalitis to multifocal demyelinating encephalitis." *Id.* at 6. She cited a study by Arnold et al.,[57] which showed that in a pediatric group with encephalitis, "5% of children showed neurologic symptoms who were infected with HMPV." *Id.* (citing Resp't's Ex. A, Tab 6, ECF No. 36-6). The authors noted that there have been reports "suggesting that HMPV may also cause disease of the [CNS] but its true role in encephalitis is not established." Resp't's Ex. A, Tab 6 at 1. They discussed nine patients "with evidence of HMPV infection and a spectrum of CNS abnormalities ranging from uncomplicated seizures to fatal encephalitis." *Id.* Dr. Gans also cited a retrospective study of patients with encephalitis by Glaser et al.,[58] which found that HMPV was the third most common respiratory pathogen causing neurologic disease in a study of 204 patients with a "possible etiologic agent[.]" Resp't's Ex. A at 6 (citing Resp't's Ex. A, Tab 11 at 6, ECF No. 37-1). Dr. Gans relied on the Arnold et al. and Glaser et al. articles to note that "the [CNS] profile is normal in the majority" of cases of HMPV infected children with neurologic diseases. *Id.* (citing Resp't's Exs. A, Tabs 6, 11); *see also* Resp't's Exs. A, Tabs 7–10, ECF Nos. 36-7–36-10.

She then discussed a case report by Schildgen et al.,[59] which described a case where a child died of encephalitis. Resp't's Ex. A at 6 (citing Resp't's Ex. A, Tab 7). The authors noted that this case "might be correlated with primary [HMPV]." Resp't's Ex. A, Tab 7 at 1. They also noted that "[a]lthough neurologic symptoms have been described for infections caused by other paramyxoviruses, such as . . . mumps and measles, no such symptoms have been associated with

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[56] *See id.*

[57] J. Arnold, et al., *Human Metapneumovirus Associated with Central Nervous System Infection in Children,* 28 PEDIATR. INFECT. DIS. 1057–60 (2009).

[58] C.A. Glaser, et al., *Beyond Viruses: Clinical Profiles and Etiologies Associated with Encephalitis,* 43 CLIN. INFECT. DIS. 1565–77 (2006).

[59] O. Schildgen, et al., *Human Metapneumovirus RNA in Encephalitis Patient,* 11:3 EMERGING INFECT. DIS. 467–71 (2005).

HMPV infection." *Id.* Nonetheless, they opined that the child in the study died from edema caused by encephalitis "probably induced or triggered by HMPV." *Id.* The child's lab results showed an elevated CSF and no other suggestions of inflammation. *Id.* No other bacterial or viral pathogens were detected, except for HMPV. *Id.* at 2. The authors determined that "while testing of the CSF was not positive for viral RNA, . . . the brain tissue tested at autopsy was positive[,] despite the child having a normal CSF profile and negative CSF [polymerase chain reaction ("PCR"),] for HMPV." *See id.* The authors also found inflammation in the lung at autopsy. *Id.* at 3. Based on this, the authors maintained they demonstrated the "first fatal encephalitis that might be associated with HMPV infection." *Id.* at 4.

Dr. Gans relied on a similar case report by Fernandez et al.,[60] wherein "both the respiratory and CSF were positive for HMPV[]" in a ten-year-old girl who developed acute encephalitis. Resp't's Ex. A at 6 (citing Resp't's Ex. A, Tab 8). The authors concluded that "[t]he detection of [HMPV] in [the CSF] strongly suggests its causative role in acute encephalitis." Resp't's Ex. A, Tab 8 at 1. They maintained this is because "it has been isolated from the respiratory tract during the acute phase of several cases of encephalitis and in postmortem lung and brain tissue of a patient with a fatal encephalitis." *Id.* Using the reports from Schildgen et al. and Fernandez et al., Dr. Gans argued that "[t]his suggests that the neurologic disease caused by HMPV may result from direct viral invasion and that the virus is not very inflammatory in the CNS[.]" Resp't's Ex. A at 6 (citing Resp't's Exs. A, Tabs 7–8). She opined "that the virus is tissue bound and not free in fluids (similar to other neuropathic viruses such as [herpes simplex virus])." *Id.*

She also cited articles by Leake et al. and Hughes et al. to note that "CNS manifestations of neurologic disease may result from a post-infectious phenomenon[.]" *Id.* (citing Resp't's Exs. A, Tabs 12–13, ECF Nos. 37-2–37-3).[61] The authors of the Leake et al.[62] article noted that "[t]he lack of evidence for ongoing infection or vaccination in most cases and the usual time lapse of a few weeks between infectious symptoms or signs and ADEM onset have promoted the view that ADEM is a postinfectious immune disease." Resp't's Ex. A, Tab 12 at 2. However, the authors also noted that "ADEM has been observed after vaccination with animal brain-derived rabies vaccines and, rarely, after administration of other vaccines." *Id.* In post-infectious cases of ADEM, the authors noted that molecular mimicry between MOG and MBP has been proposed as an explanation for the autoreactive immune responses to the CNS. *Id.* Further, the authors of the Hughes et al.[63] article found that two thirds of the patients with Guillain-Barré syndrome ("GBS") in their "two large series" studies had an infection within the previous six weeks. Resp't's Ex. A, Tab 13 at 2.

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[60] I. Sanchez Fernandez, et al., *Human Metapneumovirus in the Cerebrospinal Fluid of a Patient with Acute Encephalitis,* 69:5 ARCH. NEUROL. 649–53 (2012).

[61] J. Leake, et al., *Acute Disseminated Encephalomyelitis in Childhood: Epidemiologic, Clinical and Laboratory Features,* 23 PEDIATR. INFECT. DIS. 756–64 (2004); R. Hughes, et al., *Guillain-Barré syndrome,* 366 LANCET 1653–66 (2005).

[62] J. Leake, et al., *Acute Disseminated Encephalomyelitis in Childhood: Epidemiologic, Clinical and Laboratory Features,* 23 PEDIATR. INFECT. DIS. 756–64 (2004).

[63] R. Hughes, et al., *Guillain-Barré syndrome,* 366 LANCET 1653–66 (2005).

The authors of the Pidcock et al.[64] article found "47% of children with acute [TM] had an antecedent infectious process with onset on average 11 days prior to onset of neurologic symptoms." Resp't's Ex. A at 6 (citing Resp't's Ex. A, Tab 15, ECF No. 37-5). The authors determined that "[o]f the 13 children in the study with an antecedent immunization, 8 had signs of an antecedent illness." *See id.* They concluded that "the young age of children in their study with acute [TM] predicts that most children will have an antecedent immunization prior to symptom onset given the vaccine schedules[.]" Resp't's Ex. A, Tab 15. They continued that "together with the lack of any consistent vaccine association," this "undermine[s] a potential causal link between immunization and acute [TM]." *See id.* Dr. Gans further relied on the article by Absoud et al.,[65] which showed 66% of cases of pediatric TM were associated with an acute illness. Resp't's Ex. A at 7 (citing Resp't's Ex. A, Tab 17). Finally, she cited an article by Wolf et al.,[66] documenting an antecedent illness in 50–100% of the time prior to the onset of TM. Resp't's Ex. A at 7 (citing Resp't's Ex. A, Tab 16 at 2, ECF No. 37-6). The authors noted that "[o]ther less common provoking factors [of TM] include vaccines[.]" Resp't's Ex. A, Tab 16 at 2. They indicated that molecular mimicry is one proposed theory for the immunopathogenesis of infiltrations of the spinal cord, including TM. *Id.*

Based on the medical literature, Dr. Gans argued that "it is well supported that children who are infected with HMPV and are not vaccinated suffer from neurologic complications and thus HMPV alone is sufficient as a cause for the ADEM/TM that M.P. experienced." Resp't's Ex. E at 1. Dr. Gans wrote that there is "substantial epidemiologic and pathophysiologic data providing a causal relationship of HMPV to ADEM/TM and no data supporting a causal relationship with vaccines, solely a temporal association." *Id.* Dr. Gans maintained that the reports of vaccines preceding the onset of ADEM or TM "are temporal only with no specimens showing an actual link to disease and only speculation of how vaccines may cause demyelination." *Id.*

On the other hand, there is "support for HMPV to cause [ADEM], and that it does so alone." Tr. 152:14–21 (citing Resp't's Ex. E, Tab 1).[67] Dr. Gans opined "this clearly makes HMPV a more likely agent as a cause of ADEM/TM . . . ." Resp't's Ex. E at 1. As additional support, Dr. Gans relied on the studies performed through the Vaccine Safety Datalink. *Id.* She noted that such studies provide a "systematic review of vaccine outcomes in a full population." *Id.* In the study by Baxter et al.,[68] the authors looked at the relationship between receipt of a vaccine and the development of ADEM/TM. *Id.* at 2 (citing Resp't's Ex. E, Tab 1 at 1). The authors used a "a case-centered design, which compare[d] vaccination patterns during an exposure interval prior to the outcome in cases [versus] the entire study population, matched by age, sex, and site." *See id.* The study included 64 million vaccine doses. *Id.* Overall, the authors found that "[f]or TM, there was no statistically significant increased risk of immunization[]" in either the 5 to 28-day or the 2 to 42-day risk interval prior to onset. Resp't's Ex. E, Tab 1 at 1, 5. "For ADEM, the Tdap [] vaccine was associated with a statistically significant increase in risk in the 5 to 28-day exposure interval

[64] F.S. Pidcock, et al., *Acute Transverse Myelitis in Childhood: Center-Based Analysis of 47 Cases,* 68:18 NEUROL. 1474–80 (2007).
[65] *See* M. Absoud, et al., *supra* note 24.
[66] V. Wolf, et al., *Pediatric Acute Transverse Myelitis Overview and Differential Diagnosis,* 27:11 J. CHILD NEUROL. 1426–36 (2012).
[67] *See* R. Baxter, et al., *supra* note 47.
[68] *See id.*

. . . but not the longer 2 to 42-day interval." *Id.* The authors determined this shorter interval indicated a "possible association of ADEM with [the] Tdap vaccine[.]" *Id.* at 1.

Dr. Gans addressed the methodology used in the Baxter et al. study and noted that the authors "did[not] exclude people who had been given more than one vaccine, but they actually did[not] do their analysis to look at what happens when somebody receives measles and varicella and everything else[.]" Tr. 154:15–18. She explained "their analysis looked at [vaccines] one at a time[.]" Tr. 154:21–22. She stated her understanding is that their "analysis was not done to understand any impacts or additive effects of having more than one vaccine[.]" Tr. 155:3–9. Under my questioning, Dr. Gans agreed that "whether or not you have one vaccine or a multitude of vaccines does not increase the immunologic response that could trigger cross-reaction that would be pathogenic." Tr. 165:16–20.

Regarding the time of onset of M.P.'s neurologic symptoms, Dr. Gans opined that the temporal association of MMR and varicella vaccines "are neither necessary nor contributors to the [TM] which can be explained solely by [M.P.'s] acute viral illness." Resp't's Ex. A at 7.

On cross-examination, Dr. Gans maintained that there is "no association in large studies of live viral vaccines with [neurologic] outcomes." Tr. 163:1–2. Even when confronted with medical literature that showed "at least a potential association between the MMR vaccination and ADEM[,]" Dr. Gans testified that she does not think there is an association described in large studies. Tr. 163:7–11. She noted that she has "seen [the association] with case reports or VAERS reporting." Tr. 163:11–12. Dr. Gans explained "there[is] biologic plausibility" for the MMR vaccine to cause ADEM in the literature "because we know that the actual viruses within those [vaccines] cause ADEM." Tr. 163:16–19. Dr. Gans stated that it is her belief that there is no evidence that the MMR and varicella vaccines can cause ADEM or TM. Tr. 164:23–25. She testified she would never expect to see it happen. Tr. 165:8–10.

3. Respondent's Expert, Dr. Kruer

Dr. Kruer submitted two expert reports and testified during the entitlement hearing. *See* Resp't's Exs. C, F; Tr. 102–136. He opined that "M.P.'s ADEM/TM is far-more likely to be caused by infection than by [her] vaccination[s.]" Resp't's Ex. C at 2. Dr. Kruer considered M.P.'s human metapneumovirus to be the alternate cause that is a "much more likely" explanation for her injuries. Tr. 116:15–17, 124:16–18.

He opined that "Dr. Steinman's contention that MMR and varicella immunizations somehow caused M.P.'s ADEM is purely speculative." Resp't's Ex. C at 2. He argued that "[j]ust because something can happen does[not] mean that it did happen." Tr. 111:1–2. He wrote that there is no evidence to indicate that the administration of M.P.'s vaccinations led to her ADEM. Resp't's Ex. C at 2. He testified he "just do[es not] think that there[is] evidence that[is] nearly as compelling supporting the vaccines in question and the pathogenesis of ADEM as compared to alternate explanations that are also under consideration[]" in M.P.'s case. Tr. 116:8–12. Instead, Dr. Kruer opined that M.P. suffered from at least one, but possibly two, intercurrent infections around the time of her MMR and varicella vaccinations, and then developed ADEM. Resp't's Ex. C at 2. As support, Dr. Kruer attributed M.P.'s runny nose, cough, and fever to her HMPV infection

rather than to her ADEM. *Id.* He further noted that M.P. experienced diarrhea contemporaneously with the other symptoms. *Id.* Dr. Kruer attributed M.P.'s diarrhea to a possible second infection or her antibiotic use, and noted that ADEM neither causes this symptom nor runny nose, cough, and fever. *Id.*

Dr. Kruer addressed Dr. Steinman's claim that M.P.'s vaccinations must have been the cause of her injuries because, although her family members were sick, M.P. was the only person in her family to receive a vaccination and to develop TM and ADEM. Tr. 118:2–5. Dr. Kruer opined that "just arguing that because [M.P.'s onset of injuries] happened at that point in time, that that necessarily construed an association [with the vaccine], it just d[oes not] hold up." Tr. 118:10–12. He stated that his "most significant concern" about this contention was that "it was[not] clear to [him] that no other members of the family had received the vaccines." Tr. 118:8–10. Dr. Kruer then testified that MMR and varicella vaccinations typically provide lifelong immunity and do not require boosters. Tr. 125:5–25, 126:1–8. Under my questioning, Dr. Kruer clarified that when he indicated he did not know if M.P.'s family members had been vaccinated around the time of her HMPV infection, he was "talking about the primary series[]" of such vaccinations, not boosters. Tr. 126:9–15.

Dr. Kruer further opined that it is not necessary to invoke the vaccine as a cause of M.P.'s injuries when her infection is also a known cause of TM and ADEM. Tr. 117:2–9. As support for his opinion, Dr. Kruer relied on medical literature showing that ADEM is rarely associated with vaccination, and associations between MMR and varicella vaccinations, specifically, and ADEM is even more rare. Resp't's Ex. C at 2 (citing Resp't's Ex. C, Tab 6).[69] On cross-examination, he discussed literature showing an association between vaccinations and ADEM. He addressed the Klein et al.[70] study, which noted that ADEM is a known outcome of the MMR and/or varicella vaccines. Tr. 115:8–9 (citing Resp't's Ex. C, Tab 6 at 3). In Dr. Kruer's opinion, this article did not "show a clear signal associating the vaccines in question with ADEM." Tr. 115:19–21.

Instead, Dr. Kruer cited literature showing an association between ADEM and infections. Dr. Kruer relied on an article by Pohl,[71] which noted that ADEM is "typically preceded by an infection, and this association has been included in the definition of ADEM as a typically post-infectious entity." Resp't's Ex. C at 2 (citing Resp't's Ex. C, Tab 2, ECF No. 41-2). Dr. Kruer indicated that a study by Hynson et al.[72] showed that a precipitating infection is identified in approximately 75% of ADEM cases. *Id.* (citing Resp't's Ex. C, Tab 3 at 2, ECF No. 41-3). The authors found that of the 31 children in their study, 22 patients, or 71%, had prodromal illnesses prior to the development of ADEM, "with the majority of these being upper respiratory tract infections or nonspecific febrile illnesses." Resp't's Ex. C, Tab 3 at 2. They also noted that 2 patients, or 6%, had received the Hepatitis B vaccine three to six weeks before developing ADEM.

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[69] *See* N. Klein, et al., *supra* note 46.
[70] *See id.*
[71] D. Pohl, *Epidemiology, Immunopathogenesis and Management of Pediatric Central Nervous System Inflammatory Demyelinating Conditions,* 21 CURR. OP. NEUROL. 366–72 (2008).
[72] J.L. Hynson, et al., *Clinical and Neuroradiologic Features of Acute Disseminated Encephalomyelitis in Children,* 56 NEUROL. 1308–12 (2001).

Id. Dr. Kruer also cited a study by Menge et al.,[73] which demonstrated no association between ADEM and immunization but a strong association between antecedent infection and ADEM. Resp't's Ex. C at 2 (citing Resp't's Ex. C, Tab 7, ECF No. 41-7). The authors nonetheless concluded that "the pathogenic events that trigger the initial clinical attack [of ADEM] . . . remain unknown." Resp't's Ex. C, Tab 7 at 2.

On cross-examination, Dr. Kruer further relied on the Baxter et al.[74] article to argue that there is a more compelling association between infection and ADEM and TM compared to immunization, which has a "very weak [association with ADEM and TM] at best." Tr. 124:1–9 (citing Resp't's Ex. E, Tab 1). Dr. Kruer argued that "the preponderance of evidence[, based on the papers discussed during the hearing,] indicate[s] that ADEM is simply more commonly, more typically associated with a preceding infection, and that, in fact, if there is a signal for ADEM after vaccination, it[is] actually a rare occurrence." Tr. 120:1–5.

Dr. Kruer addressed Dr. Steinman's theory pursuant to *Althen* prong one. Dr. Kruer wrote that while he "agree[s] with most of Dr. Steinman's statements[,]" he "believe[s] there are fallacies in [Dr. Steinman's] reasoning and thus his contentions are not logically supported." Resp't's Ex. F at 1. Dr. Kruer argued that the BLAST results "do not establish molecular mimicry." Resp't's Ex. C at 2. He described molecular mimicry as "something that does require a degree of sequence homology but that also requires evidence of an autoreactive response that was directly related to that homology." Tr. 109:13–16. Dr. Kruer explained that "[t]riggering an autoimmune response not only requires sequence homology, it [also] requires that the responsible protein be taken up and processed by antigen-presenting cells[.]" Resp't's Ex. C at 3. The protein must then be "cleaved to generate the theorized peptides, . . . outcompete the thousands of other peptide combinations produced to [] stimulate the generation of autoreactive T and/or B-cell clones," which then "help direct the immune response." *Id.* (citing Resp't's Ex. C, Tab 10, ECF No. 41-10).[75]

He further argued that Dr. Steinman's "arbitrary criteria" to define a meaningful molecular mimic as "a run of 5 or more of 12 amino acids that are identical" is "not widely accepted in the scientific community." *Id.* at 2 (citing Pet'r's Ex. 19 at 7). He argued that the "degree of sequence homology that Dr. Steinman shows is inconsequential[.]" *Id.* at 3. Dr. Kruer opined that the "criterion does not stand up to further scrutiny." *Id.* He continued "[g]iven that there are only 20 possible characters in the amino acid 'alphabet,' and that most proteins are several hundred amino acids long, when one applies a moving window analysis, possibilities abound for matching peptide sequences." *Id.* He relied on an article by O'Brien et al.[76] to note that "the optimal epitope length needed to maximally activate T-cells via MHC receptors is 18–20 amino acids long[], 12–15 residues for CD4+ T cell recognition of MHC Class II, and shorter peptides of 7–9 residues for MHC I and CD8+ T-cells." *Id.* at 2–3 (citing Resp't's Ex. C, Tab 9, ECF No. 41-9).

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[73] T. Menge, et al., *Acute Disseminated Encephalomyelitis: An Acute Hit Against the Brain,* 20 CURR. OP. NEUROL. 247–54 (2007).
[74] *See* R. Baxter, et al., *supra* note 47.
[75] J. Fourneau, et al., *The Elusive Case for a Role of Mimicry in Autoimmune Diseases,* 40 MOLECULAR IMMUNOL. 1095–102 (2004).
[76] C. O'Brien, et al., *Peptide Length Significantly Influences in vitro Affinity for MHC Class II Molecules,* 4:6 IMMUNOME RES. 1–7 (2008).

As additional support, Dr. Kruer cited an article by Kanduc et al.,[77] which "analyzed viral proteins and compared them to the [approximately] 30,000 known human proteins[.]" *Id.* at 3 (citing Resp't's Ex. C, Tab 14, ECF No. 40-4). The authors found a total of 2,907,096 matches of 5 amino acid residues. *See id.* Based on this article, Dr. Kruer opined "it is not surprising that Dr. Steinman was able to find a handful of matches in his own BLAST searches." Resp't's Ex. C at 3. Dr. Kruer further noted that when humans become ill with viral infections, on average multiple times per year, it is reflected by ≥5 amino acids in a stretch of homology. *Id.* He opined that "[i]f all that was required to induce autoimmunity was such sequence overlap, 100% of the population should be afflicted with an autoimmune disease. Yet this is clearly not the case." *Id.* Similarly, Dr. Kruer testified, consistent with his written report, that "there are 3,713,010 matches of human proteins with themselves." Tr. 111:12–17 (citing Resp't's Ex. C at 3). He opined that "[a]gain, if all that was required for autoimmunity was sequence homology, infection should not even be needed to trigger autoimmunity; one's own body should provide ample opportunity for autoimmunity to develop." Resp't's Ex. C at 3. He therefore argued that "just because Dr. Steinman was able to show there[is] a degree of homology between two things, this [statistic] is an example that there are literally more than 3 million other peptides that show such homology." Tr. 111:23–25, 112:1.

Dr. Kruer addressed Dr. Steinman's conclusion regarding the immunity to nervous system proteins including myelin in healthy individuals despite the fact that most healthy people do not suffer from autoimmune diseases. Resp't's Ex. F at 1. Dr. Kruer wrote that he "completely agree[s] . . . [and] that is exactly [his] point." *Id.* Dr. Kruer explained that "[i]f peptide homology were the only factor that was necessary to trigger autoimmunity, then even innocuous exposures like green beans, could wantonly elicit a state of autoimmunity in otherwise healthy people." *Id.* He used this analogy to "drive home the point that more than molecular mimicry is necessary for autoimmune disease (like [TM] and/or ADEM) to actually occur." *Id.* He noted that Dr. Steinman agrees with him on this point and "thus undermines [Dr. Steinman's] own argument[.]" *Id.*

Then, Dr. Kruer attacked Dr. Steinman's BLAST searches and their relevance to M.P.'s case. Resp't's Ex. C at 3. Dr. Kruer posited that "[c]omputer-based simulations are simply not able to predict whether any of these peptides stimulated autoimmunity in M.P.'s case." *Id.* Dr. Kruer opined that Dr. Steinman's method "only goes so far[]" and his "subsequent conclusions went beyond what was able to be demonstrated solely by a BLAST search." Tr. 110:16–20. Dr. Kruer posited that while Dr. Steinman's BLAST searches "indicate limited sequence homology[,]" they "do nothing to show that these theoretical peptides w[ould] actually be produced, let alone incite an autoimmune response." Resp't's Ex. C at 2.

Dr. Kruer continued that "even if one overlooks the oversimplified criteria for molecular mimicry that [Dr. Steinman] presents, and assumes that molecular mimicry were . . . triggered by vaccine exposure[,]" in M.P.'s case, "the most that this sequence of events would lead to is a situation where M.P. would have autoreactive B- and/or T-cells circulating in her body." Resp't's Ex. F at 1. He maintained that Dr. Steinman agreed that "this has been shown to be necessary but not sufficient T [cell involvement] for autoimmune disease to result." *Id.*

[77] D. Kanduc, et al., *Massive Peptide Sharing Between Viral and Human Proteomes,* 29 PEPTIDES 1755–66 (2008).

Dr. Kruer opined that to prove the relationship between the vaccines at issue and M.P.'s injuries, he would "require homology and an autoreactive response, and the homology and autoreactive response need to be from the inciting peptide to the insuming [sic] target of reactivity." Tr. 120:19–25, 121:1–3. The target of reactivity is "against a specific relevant . . . brain protein." Tr. 121:3–4. He indicated that "it is true that anti-[MBP] and anti-[MOG] autoantibodies are present in a fraction of ADEM cases." Resp't's Ex. C at 3 (citing Resp't's Exs. C, Tabs 11–12, ECF Nos. 40-1–40-2).[78] Dr. Kruer relied on an article by Ramanathan et al.[79] to argue that "[i]t is not clear that these autoantibodies cause disease in and of themselves, even when present." *Id.* (citing Resp't's Ex. C, Tab 13, ECF No. 40-3). Dr. Kruer testified that "anti-MOG antibodies are not invariably present. There are some cases that have them; there are some that do[not]." Tr. 121:20–22. He noted that M.P. "was never shown to have autoantibodies to any of the proteins Dr. Steinman BLAST[ed]," therefore, the BLAST searches do not "conclusively show sequence homology to proteins known to be relevant to this case." Resp't's Ex. C at 3. Dr. Kruer testified that additional supporting evidence of this reaction in M.P. would have been to do a blood or spinal fluid test for anti-MOG antibodies at the time of an active response. Tr. 121:16–20, 122:11–17. He noted that this testing was not performed in M.P.'s case. Tr. 122:20–23.

To substantiate his argument that establishing sequence homology does not show evidence of a cross-reaction, Dr. Kruer ran his own BLAST search. Resp't's Ex. C at 3; Tr. 113:14. He posited that by the age that M.P.'s ADEM occurred, "[m]ost children in the U.S. have been eating baby foods for several months" and "are thus exposed to a host of new proteins that occur as natural components of these new foods." Resp't's Ex. C at 3. Dr. Kruer then BLASTed a green bean protein versus MBP. *Id.* He explained that he BLASTed the protein portion of the green bean to show that limited sequence homology, is "hardly a remarkable thing." Tr. 113:15–16. He opined, "[i]t[is] actually very, very common when comparing two proteins or portions of a protein[.]" Tr. 113:16–18. He found sequence homologies in three places "of 5, 6, and 7 amino acids in a 12 residue stretch between green bean protein and [MBP]." Resp't's Ex. C at 4. Based on these results, Dr. Kruer argued that by Dr. Steinman's standards, "it is just as likely that green beans caused M.P.'s ADEM as it is that her MMR and varicella vaccines were to blame." *Id.* at 4–5. Dr. Kruer stated that the green bean example "was meant to illustrate that there are many, many proteins that could show a similar degree of sequence homology." Tr. 114:16–19. He concluded it showed that just because Dr. Steinman could prove a sequence homology, it does not mean molecular mimicry occurred in this case. Tr. 114:22–25.

On cross-examination, Dr. Kruer stated it is "possible" for the MMR and varicella vaccines to trigger ADEM and TM. Tr. 120:9–18. However, he maintained that it is not likely that the vaccines are related to M.P.'s injuries. Tr. 123:21–23.

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[78] K. van Haren, et al., *Serum Autoantibodies to Myelin Peptides Distinguish Acute Disseminated Encephalomyelitis from Relapsing-Remitting Multiple Sclerosis,* 19:13 MULTIPLE SCLEROSIS J. 1726–33 (2013); M. Baumann, et al., *Clinical and Neuroradiological Differences of Paediatric Acute Disseminating Encephalomyelitis with and without Antibodies to the Myelin Oligodendrocyte Glycoprotein,* 86 J. NEUROL. NEUROSURG. PSYCH. 265–72 (2015).

[79] S. Ramanathan, et al., *Anti-MOG Antibody: The History, Clinical Phenotype, and Pathogenicity of a Serum Biomarker for Demyelination,* 15 AUTOIMMUN. REV. 307–24 (2016).

IV. Applicable Legal Standards

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) the petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at 42 U.S.C. § 300aa-14, as amended by 42 C.F.R. § 100.3; or (2) that petitioner suffered an "off-Table injury," one not listed on the Table, as a result of his receiving a covered vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner alleges that M.P. suffered from encephalitis, which is a Table injury for the MMR vaccination.[80] Thus, Petitioner must prove that M.P.'s encephalitis meets the Table criteria for that injury.

Petitioner also alleges that M.P.'s ADEM and TM were caused-in-fact by the vaccines at issue. To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. 42 U.S.C. § 300aa-13(a)(1)(A). A petitioner is required to prove that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)).

In the seminal case of *Althen v. Sec'y of the Dept. of Health & Hum. Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires petitioners to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *Id.* "[T]hese prongs must cumulatively show that the vaccination was a 'but-for' cause of the harm, rather than just an insubstantial contributor in, or one among several possible causes of, the harm." *Pafford v. Sec'y of Health & Hum. Servs.,* 451 F.3d 1352, 1358 (Fed. Cir. 2006). "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280. Further, evidence used to satisfy one prong of the test may overlap to satisfy another prong. *Capizzano,* 440 F.3d at 1326.

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs*., 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994). In such a case, the government must not merely prove the existence of an alternative cause, but that such an alternative actually caused the injury. *Knudsen,* 35 F.3d at 549. Consequently, when and if a petitioner establishes a prima facie case, the burden then shifts to the

[80] Petitioner does not allege, nor does the evidence support, a Table claim for injuries sustained as a result of M.P.'s varicella vaccination. *See* Am. Pet. at 2.

government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1354 (Fed. Cir. 2008); *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that the respondent's burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" 42 U.S.C. § 300aa-13(a)(2); *see also Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (explaining that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

In considering the reliability of a petitioner's evidence of a prima facie case, the special master may consider alternative causes for a petitioner's condition that are reasonably raised in the record, even if the respondent does not pursue a formal alternative cause argument. *Doe,* 601 F.3d at 1358. This is especially true where there are multiple factors acting in concert, and the "causative effect" of the vaccine may be "overwhelmed" by competing alternative causes. *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1151 (Fed. Cir. 2007) ("Where multiple causes act in concert to cause the injury, proof that the particular vaccine was a substantial cause may require the petitioner to establish that the other causes did not overwhelm the causative effect of the vaccine"); *see also Shyface,* 165 F.3d at 1352. Thus, in weighing a petitioner's case-in-chief, a special master may consider evidence that the petitioner's alleged injury could have been caused by alternative causes. *Walther*, 485 F.3d at 1151. Proof of a "logical sequence of cause and effect" will eliminate potential likely alternatives. *Id*.

V. Discussion

A. Experts

Although special masters have the discretion to be informed by past rulings and experiences, case-specific filings and testimony are the most helpful types of evidence, given the fact-specific nature of each decision. *See Doe v. Sec'y of Health & Hum. Servs.*, 76 Fed. Cl. 328, 338–39 (2007). To that end, experts are an essential piece of a petitioner's claim and Respondent's defense. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000)). This case ultimately turns, not only on M.P.'s medical history, but also the persuasiveness of the written reports, supporting documentation, and expert testimony. I therefore must assess each expert's opinion and assign weight accordingly. This assessment will inform my analysis pursuant to each prong of *Althen*.

Indeed, all three experts have extensive experience and impressive credentials in neurology, immunology, and demyelinating diseases, such as TM and ADEM. *See, e.g.*, Pet'r's Ex. 20; Resp't's Exs. B, D. However, Dr. Steinman delivered his testimony with fewer equivocations than both of Respondent's experts. While Drs. Gans and Kruer have provided useful testimony and persuasive explanations in previous cases before me, as well as other special masters in the Program, presently, Drs. Kruer and Gans presented their opinions riddled with assumptions, reversals, and concessions when compared to Dr. Steinman's analysis. *See Broekelschen*, 618 F.3d

at 1347 (citing *Lampe*, 219 F.3d at 1362) (finding that where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories"). For instance, Dr. Kruer strongly disagreed with Dr. Steinman's assumption that no other members of M.P.'s family received MMR or varicella vaccines around the time M.P. and her family became ill. Dr. Kruer then acknowledged that MMR and varicella vaccinations typically have lifelong immunity and do not require boosters. Despite this acknowledgment, he maintained that he does not know for sure that M.P.'s family members did not receive the primary series of such immunizations at the same time as M.P.'s vaccinations. Tr. 125:5–25, 126:1–15. It is generally well-accepted that the primary series of MMR and varicella vaccinations are administered during early childhood (ranging from 12 to 15 months of age).[81] Therefore, I find it is not more likely that M.P.'s older family members received the primary series of MMR or varicella vaccinations at the same time as M.P. Dr. Kruer's argument that M.P.'s vaccinations played no role in causing her condition is undercut by his reliance on the unsupported assumption that her family was also vaccinated without adverse effect.

Likewise, Dr. Gans repeatedly demonstrated a reluctance to acknowledge any probative value of certain evidence. When confronted with the body of medical literature submitted by Petitioner that shows a potential association between the MMR vaccination and ADEM, she testified that "[t]here[has] been no association in large studies of live viral vaccine with these outcomes." Tr. 163:1–2. She later acknowledged that she has "seen it with case reports or VAERS reporting." Tr. 163:11–12. However, she opined that these individual instances are only evidence of "biologic plausibility" for the MMR vaccine to cause ADEM in the literature. Tr. 163:12–15. Dr. Gans then hedged in her discussion of the impact of a primary versus secondary exposure to the HMPV infection on M.P.'s immune system. Dr. Gans testified that "the most important thing that you[are] seeing here is not that M.P. had vaccines[; i]t[is] that M.P. never saw human metapneumovirus before." Tr. 168:7–10. During that same line of questioning, Dr. Gans later stated "because of the way that people respond to things, whether first, second, third, I think that if M.P. was going to have a more severe reaction to this virus, she would have a more severe reaction anytime[.]" Tr. 172:17–21. While Dr. Gans has specific and relevant knowledge regarding a child's immune response to vaccines, the main focus of her testimony was a discussion of the medical literature that was largely unhelpful. When considering the parties' arguments in relation to the biological mechanism and immunologic response involved in M.P.'s demyelinating conditions, Dr. Steinman's delivery contributed significantly more to the value of his testimony than Drs. Kruer and Gans.

B. Petitioner's Table Claim

Pursuant to the Table (in January of 2018, at the time the amended petition was filed), encephalitis is a compensable injury if the first symptoms thereof occurred within 5 to 15 days after the administration of the MMR vaccine. 42 U.S.C. § 300aa-14(a). In general, to succeed on such a claim, a petitioner would need to establish that the injured party experienced an acute encephalitis as defined by the Qualifications and Aids to Interpretation ("QAIs"). 42 C.F.R. § 100.3(c)(3) (2018). The QAIs indicate that a petitioner must show evidence of an acute encephalitis within the applicable time period that results in chronic encephalopathy. *See id.* Acute encephalitis

[81] *See Child and Adolescent Immunization Schedule,* CENTER FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html (last visited July 29, 2022).

is demonstrated by evidence of neurologic dysfunction plus evidence of an inflammatory process in the brain. § 100.3(c)(3)(i). Evidence of neurologic dysfunction consists of either: one neurologic finding referable to the CNS, including "[f]ocal cortical signs ([] aphasia, alexia agraphia, cortical blindness), cranial nerve abnormalities, visual field defects, abnormal presence of primitive reflexes . . . or cerebellar dysfunction ([] ataxia, dysmetria, or nystagmus);" or an acute encephalopathy. *See* §§ 100.3(c)(3)(i)(A)(1)–(2). An acute encephalopathy for children less than 18 months old who did not suffer a seizure "is indicated by a significantly decreased level of consciousness that lasts at least 24 hours." § 100.3(c)(2)(i)(1). Evidence of an inflammatory process in the brain must include "[CSF] pleocytosis (>5 [WBC]/mm^3 in children >2 months of age and adults; >15 WBC/mm^3 in children <2 months of age)" or at least two of the following: "fever (temperature ≥ 100.4 degrees Fahrenheit); electroencephalogram findings consistent with encephalitis . . . or neuroimaging findings consistent with encephalitis, which include [] brain/spine [MRI] displaying diffuse or multifocal areas of hyperintense signal on T2 weighted, diffusion-weighted image, or fluid-attenuation inversion recovery sequences." §§ 100.3(c)(3)(i)(B)(1)–(3).

The QAIs also include exclusionary criteria for establishing a Table claim of encephalitis. If the encephalitis was caused by either an underlying malignancy that led to paraneoplastic encephalitis; an infectious disease associated with encephalitis, such as a bacterial, parasitic, fungal, or viral illness; ADEM (confirmed with findings on MRI distinctly showing evidence of acute demyelination), or any other abnormality that would explain the symptoms, the vaccinee shall not be entitled to compensation. §§ 100.3(c)(3)(ii)(A)–(D).

A Table injury of encephalitis was alleged in Petitioner's amended petition filed on January 30, 2018, and there is no dispute that Petitioner meets the Table criteria with respect to the onset and symptomology of M.P.'s injury. However, Petitioner previously acknowledged during a status conference on January 29, 2018, that ADEM is among the exclusionary criteria for encephalitis on the Table. *See* Sched. Order at 2, ECF No. 51. Petitioner also admitted that M.P.'s encephalitis was shown to be caused by ADEM. *Id.*; Pet'r's Ex. 5 at 162. In a later status conference on April 17, 2018, I told the parties that the medical records do not seem to support an encephalitis Table injury. Sched. Order at 1, ECF No. 58. In response, Petitioner stated she intended to proceed on a claim of causation-in-fact. *Id.* In light of M.P.'s disqualifying ADEM and Petitioner's confirmation that she is only asserting a causation-in-fact claim, a more detailed discussion of Petitioner's Table encephalitis claim is not required. Petitioner is unable to establish entitlement to compensation based on a Table claim of encephalitis.

C. Petitioner's Causation-in-Fact Claim – *Althen* Prong One

Under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question: "can the vaccine[] at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. denied*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548. Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 548–49. A petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano,* 440 F.3d

at 1325 (quoting *Althen*, 418 F.3d at 1280). Scientific and "objective confirmation" of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278–81; *see also Moberly*, 592 F.3d at 1322. However, as the Federal Circuit has made clear, "simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Rather, "[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." *Moberly*, 592 F.3d at 1322. In general, "the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged." *LaLonde,* 746 F.3d at 1339.

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe*, 219 F.3d at 1361. The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id*. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("[U]niquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). And nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

Petitioner has met her burden under *Althen* prong one. Petitioner posited a scientific or medical theory explaining the MMR and varicella vaccines' role in the development of TM and ADEM via molecular mimicry. Both parties in this case generally agree that such conditions can be autoimmune in nature. *See, e.g.*, Tr. 50:1–3, 21–23. While Respondent's experts attempted to discredit Petitioner's theory of molecular mimicry as a valid mechanism, Respondent's own submitted medical literature recognizes that molecular mimicry is a proposed mechanism for spinal cord inflammation and the development of TM. Resp't's Ex. A, Tab 16 at 2;[82] Resp't's Ex. A, Tab 17 at 4;[83] *see also* Tr. 68:17–23.

Supplemental support for Petitioner's proposed biological mechanism is found in Petitioner's submitted literature documenting a case of EAE, an animal model of ADEM induced through immunization, wherein mice exhibited T-cell and monocyte involvement post rabies vaccination but prior to the development of neurologic complications of the CNS. Pet'r's Ex. 51 at 1.[84] Dr. Steinman's note that "EAE is an experimental model of ADEM involving TM" is helpful and consistent with the Dorland's definition for EAE. Dorland's states that EAE is "an animal

[82] *See* V. Wolf, et al., *supra* note 66.
[83] *See* M. Absoud, et al., *supra* note 24.
[84] *See* L. Steinman, *supra* note 22.

model for [ADEM,] in which the characteristic pathophysiology and clinical signs of this disease are produced by immunization of an animal with extracts of brain tissue or with [MBP] together with Freund adjuvant[.]" *Dorland's* at 614; *see also* Pet'r's Ex. 19 at 5. Dr. Steinman has therefore credibly demonstrated why the conditions would be similar in pathogenesis. This literature discusses the relationship between a rabies vaccination and the subsequent development of ADEM via Petitioner's proposed biological mechanism instead of the vaccinations at issue here. However, I do not find this difference to be fatal to Petitioner's case, because absolute certainty is not the standard in the Program. *Capizzano,* 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). The same article also indicates that CNS abnormalities can arise following illness with the wild measles virus. *See* Pet'r's Ex. 51 at 1. Dr. Steinman stated that his biological mechanism does not change depending on whether the vaccine contained a live virus or not. *See* Tr. 75:8–18. Dr. Gans noted that the MMR vaccine can cause ADEM because the actual viruses contained in the vaccine are possible causes of ADEM. Tr. 163:16–19. It follows that the receipt of an MMR vaccine against measles could result in the same neurologic complications as exposure to the wild virus. This is supported by both parties' expert testimony. Respondent is otherwise unable to rebut Petitioner's overarching theory of molecular mimicry, as the medical literature submitted by both parties shows the concept is generally accepted as a proposed mechanism for the post-vaccination development of TM and ADEM.

Additionally, while prior decisions of special masters are not binding on my analysis, it is persuasive that molecular mimicry has been accepted in the Program as a biological mechanism involving demyelinating conditions, including TM and ADEM. *See, e.g.*, *Roberts v. Sec'y of Health & Hum. Servs.,* No. 09-427V, 2013 WL 5314698 (Fed. Cl. Spec. Mstr. Aug. 29, 2013); *Schmidt v. Sec'y of Health & Hum. Servs.,* No. 07-20V, 2009 WL 5196169 (Fed. Cl. Spec. Mstr. Dec. 17, 2009); *Hargrove v. Sec'y of Health & Hum. Servs.,* No. 05-0694V, 2009 WL 1220986 (Fed. Cl. Spec. Mstr. Apr. 14, 2009). It is also instructive that special masters have determined that the Prevnar-13 vaccine can cause GBS, a similar demyelinating condition, via molecular mimicry. *See, e.g.*, *Pierson v. Sec'y of Health & Hum. Servs.*, No. 17-1136V, 2022 WL 322836 (Fed. Cl. Spec. Mstr. Jan. 19, 2022); *Koller v. Sec'y of Health & Hum. Servs.,* No. 16-439V, 2021 WL 5027947 (Fed. Cl. Spec. Mstr. Oct. 8, 2021). In these cases, petitioners relied on the comparison between related demyelinating conditions, such as MS and GBS in place of the alleged injury of TM, to meet their burdens with respect to prong one. Petitioner did the same here with EAE.

In his reports and testimony, Dr. Steinman posited that there were molecular mimics between the components of the MMR and varicella vaccines and MOG and MBP, which are the known targets of the CNS in demyelinating conditions, including ADEM and TM. Dr. Steinman relied on literature which shows that the immune response in ADEM/TM is targeted at MBP and MOG in the CNS. Abramsky et al.[85] noted that MBP is a major protein of the myelin sheath, which is one of the targets of the immune system in TM. Pet'r's Ex. 45 at 3; Tr. 54:20–25. Similarly, Zamvil et al.[86] indicated that one of the known targets of TM is MOG. Pet'r's Ex. 48 at 1; Tr. 57:11–16. O'Connor et al.[87] found that MOG is targeted in ADEM. Pet'r's Ex. 46 at 2; Tr. 55:2–6. Van Haren et al.[88] explained that autoantibodies to defend components of myelin in ADEM

[85] *See* O. Abramsky & D. Teitlebaum, *supra* note 25.
[86] *See* S. Zamvil & A. Slavin, *supra* note 28.
[87] *See* K. O'Connor, et al., *supra* note 26.
[88] *See* K. van Haren et al., *supra* note 27.

include MOG and MBP antibodies. Pet'r's Ex. 47; Tr. 56:18–25. The body of literature submitted therefore supports that the BLAST searches Dr. Steinman ran, between these specific myelin proteins and the components of the vaccines, and the mimics he found are relevant to the diseases in question. In fact, Respondent conceded that anti-MBP and anti-MOG autoantibodies are present in ADEM cases. *See* Resp't's Ex. C at 3; Resp't's Exs. C, Tabs 11–12. Dr. Kruer argued against the relevance of these specific myelin proteins because such autoantibodies were never tested for or detected in M.P. *See, e.g.*, Resp't's Ex. C at 3. However, Dr. Kruer's argument speaks to *Althen* prong two. Therefore, Respondent has not negated the relevance of such myelin proteins in Petitioner's proposed biological mechanism.

Dr. Steinman's theory that mimics between components of the MMR and varicella vaccines, HMPV, and MOG and MBP could trigger a "perfect storm" resulting in ADEM and TM, is well supported by the record. The eleven BLAST searches performed by Dr. Steinman demonstrate that there are homologies between each of the individual components of both the vaccines at issue, HMPV, and MOG and MBP, the known points of attack in ADEM and TM. Dr. Steinman's BLAST searches therefore provide potential for the cross-reaction between the components of the vaccines at issue, HMPV, and the CNS. While Dr. Steinman did not directly identify MBP and/or MOG as components of the vaccines at issue in this case, Petitioner's theory does not need to go that far to be successful. Dr. Steinman demonstrated the existence of ample potential molecular mimics between the known components of the vaccines and MBP and MOG. *See Knudsen*, 35 F.3d at 548; *Capizzano,* 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280).

Of the eleven BLAST searches, Dr. Steinman concluded that each search met his threshold, "line in the sand" minimum sequence length for a sufficient molecular mimic because they all showed homologies in a stretch of at least 5 out of 12 amino acids. *See* Pet'r's Ex. 19 at 10–28; Tr. 60:20–25, 61:1. Dr. Steinman's conclusion is worthy of consideration. Indeed, the vast majority of his BLAST searches on the individual components of each vaccine and HMPV, versus MOG and MBP show homologies (either identical or positive close matches) of at least 7 out of 12 amino acids as Dr. Steinman contended. *See* Pet'r's Ex. 19 at 10–28. However, several of Dr. Steinman's findings were based on homologies within stretches of amino acids shorter than 12.[89]

I find the articles by Gautam et al.[90] support Dr. Steinman's assertion that even homologies in stretches of 4 of 11 amino acids, 5 of 11 amino acids, and 5 of 6 amino acids can be sufficient to induce neuroinflammation in an animal model of EAE. Pet'r's Exs. 52–54. Respondent's argument that such sequence lengths are not enough to induce neuroinflammation is not persuasive given the articles submitted by Dr. Steinman. Dr. Kruer relied on the O'Brien et al.[91] article, which shows that a homology of 12 out of 15 or 18 out of 20 amino acids is necessary to show a molecular mimic. *See* Resp't's Ex. C, Tab 9. However, the minimum sequence length described in the articles

[89] For instance, his BLAST search of the large protein of the mumps strain Jeryl Lynn in the MMR vaccine versus MBP found that in a stretch of 10 amino acids, there were 6 identical acids between MBP and this component of the MMR vaccine. Pet'r's Ex. 19 at 18–19. His BLAST of the glycoprotein from the OKA strain in the varicella vaccine versus MOG found that in a stretch of 9 amino acids, 5 homologies. *Id.* at 23–24. Similarly, Dr. Steinman's BLAST search of the thymidylate kinase from the OKA strain in the varicella vaccine versus MOG revealed overall 6 homologies in a stretch of 11 amino acids. *Id.* at 24–25.
[90] *See supra* note 38.
[91] *See* C. O'Brien, et al., *supra* note 76.

by Gautam et al. as capable of producing neuroinflammation has previously been accepted in the Program. *See, e.g.*, *E.M. v. Sec'y of Health & Hum. Servs.,* No. 14-753V, 2021 WL 3477837, at *42 (Fed. Cl. Spec. Mstr. July 9, 2021). I will likewise credit the results of Dr. Steinman's BLAST searches as evidence of molecular mimicry between each of the components of the MMR and varicella vaccines, HMPV, and the myelin proteins attacked in the diseases at issue in this case.

Furthermore, Dr. Steinman's theory involving molecular mimicry has been accepted in numerous Program cases as an accepted scientific or medical theory in the context of targeted BLAST searches. For example, in *White v. Sec'y of Health & Hum. Servs.*, the special master credited Dr. Steinman's molecular mimicry theory and supporting BLAST searches and determined that there were "sufficient homologies between the basic myelin protein and two of the strains of the HPV L1 strains . . . and between MOG and all four HPV antigens in the vaccine[,]" which could cause TM. No. 15-1521V, 2019 WL 7563239, at *24 (Fed. Cl. Spec. Mstr. Dec. 19, 2019). In that case, like Petitioner's, Dr. Steinman directed his searches to specific proteins that are "known to be targets of the immune response in [TM]," which, the special master found provided "a sound foundation for the theory of molecular mimicry." *Id.*

Respondent's attacks on the homologies revealed by Dr. Steinman's BLAST searches are unconvincing. Dr. Kruer relied on the Kanduc et al.[92] article to argue that the findings from the BLAST searches are "inconsequential" because there are "2,907,096 matches of 5 amino acid residues" within the approximately 30,000 known human proteins. Resp't's Ex. C at 3; Resp't's Ex. C, Tab 14. Dr. Kruer argued that finding homologies of 5 amino acids is therefore common. While this may be true, this does not detract from the significance of Dr. Steinman's findings. Indeed, Dr. Steinman found homologies between components of the vaccinations at issue and the relevant proteins attacked in TM and ADEM. As absolute certainty is not the standard in the Program, I am not persuaded by Dr. Kruer's argument that Dr. Steinman's findings are too common to be of consequence. *See Knudsen*, 35 F.3d at 548–49.

Respondent additionally argued that just because Dr. Steinman identified mimics between the components of the MMR and varicella vaccines, with HMPV, and MOG and MBP, such mimics do not establish that there was cross-reaction or an autoimmune response in M.P.'s case. *See, e.g.*, Resp't's Ex. C at 2–3; Tr. 109–112. He maintained that more would have to be shown to prove a cross-reaction. *See id.* However, such attacks pertain to *Althen* prong two and are not applicable to Respondent's arguments pursuant to *Althen* prong one. Additionally, Dr. Kruer conceded that the MMR and varicella vaccines can cause ADEM and TM. Tr. 120:9–18. Respondent has been unable to persuasively refute Petitioner's proposed biological mechanism.

While Petitioner did not provide literature specifically addressing whether the MMR and/or varicella vaccines can cause ADEM and TM via molecular mimicry, petitioners are not required to provide such literature to prove their claims. *See Capizzano,* 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280) (finding that a petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities[]"). After consideration of Dr. Steinman's expert opinion, I find there exists sufficient homology between the vaccines at issue and HMPV, and the key myelin

[92] *See* D. Kanduc, et al., *supra* note 77.

proteins known to be targeted in the CNS in ADEM and TM, to cause molecular mimicry and produce neuroinflammation. Petitioner has therefore satisfied prong one of *Althen*.

D. *Althen* Prong Two

Under the second prong of *Althen*, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). The special master in *Pafford* noted petitioners "must prove [] both that her vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination." 2004 WL 1717359, at *4 (citing *Shyface*, 165 F.3d at 1352). Thus, petitioners have the burden of showing that the vaccine was a substantial factor in causing the alleged injury. *Shyface*, 165 F.3d at 1353. A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec'y of Health & Hum. Servs.,* 9 F.3d 958, 961 (Fed Cir. 1993) (citation omitted). Nevertheless, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress . . . ." *Capizzano*, 440 F.3d at 1325–26.

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Id.* at 1326 (citing *Althen*, 418 F.3d at 1280). Indeed, when reviewing the record, a special master must consider the opinions of treating physicians. *Capizzano*, 440 F.3d at 1326. This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). While a special master must consider these opinions and records, they are not "binding on the special master or court." 42 U.S.C. § 300aa-13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.* The record often includes "evidence of possible sources of injury" that can show alternate causes for the alleged vaccine-related injury. *See Stone v. Sec'y of Health & Hum. Servs.,* 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."). Indeed, consideration of alternative causes in a petitioner's case-in-chief does not improperly shift the burden to a petitioner to rule out alternative causes, but rather logically allows a special master to weigh evidence in the record of alternative causes as one factor in determining whether a petitioner has established her prima facie case by

preponderant evidence. *Doe,* 601 F.3d at 1358; *see also Stone,* 676 F.3d at 1379; *Hammit,* 98 Fed. Cl. at 726.

Petitioner's expert has presented a logical sequence of cause and effect showing that M.P.'s May 14, 2015 vaccinations were a substantial factor in the development of her ADEM and TM. This case is similar to *Shyface*, wherein a baby was vaccinated with the whole-cell DPT vaccination at the time he was beginning to fight off an *E. coli* infection. *See* 165 F.3d at 1345. Both the DPT and the *E. coli* infection could and did cause fever, which rose to 110 degrees and resulted in the baby's death four days later. *Id.* Respondent defended the case and argued that the *E. coli* infection was the sole cause of the baby's fever and death. The testimony from the petitioner's treating physician showed that both the vaccine and the infection were equally responsible for the baby's fever and death. The Federal Circuit held that each of the two factors, the vaccine and the infection, was a substantial factor in causing the baby's high fever and death, and but-for the vaccination, the baby would not have had the high fever and would not have died. *See id.* The Federal Circuit ruled in favor of the petitioner though the petitioner did not prove that the DPT vaccine was the only or predominant cause of the baby's death. *Id*. at 1353.

In this case, Dr. Steinman provided preponderant evidence that M.P. would not have developed ADEM or TM but-for the vaccinations at issue. The administration of M.P.'s May 14, 2015 MMR and varicella vaccines while her body was preparing to fight off an HMPV infection resulted in a "perfect storm." Even though M.P. experienced a contemporaneous HMPV infection capable of triggering ADEM and TM alone, the vaccinations, by preponderant evidence, were a substantial factor in causing her injuries.

Indeed, Petitioner's support for *Althen* prong two is based, in part, on the application of Dr. Steinman's demonstrated molecular mimics between the vaccinations M.P. received, her HMPV infection, and the proteins targeted in the CNS in TM and ADEM. Such mimics provide sufficient support for Petitioner's theory of causation, in which the vaccinations and M.P.'s HMPV infection were both substantial factors in causing her injuries. While M.P.'s clinical testing did not include testing for autoantibodies to MBP and/or MOG to show definitive evidence of a cross-reaction, it does provide preponderant evidence that the homologies Dr. Steinman found resulted in neuroinflammation in M.P.'s case. Dr. Steinman's reliance on the findings from M.P.'s May 30, 2015 brain and spinal cord MRI results, which showed evidence of long segment involvement in the spinal cord with abnormalities from her brain stem to thoracic level 10 with vague cord enhancement, is compelling. *See* Tr. 32:6–10. This MRI also showed bilateral symmetrical periventricular T2 hyperintensities, a subtle area of T2 hyperintensity, and T1 hypointensity in the corpus collosum. Tr. 33:2–5; Pet'r's Ex. 5 at 162. Dr. Steinman credibly testified that M.P.'s MRI was consistent with neuroinflammation in the form of ADEM, and abnormalities consistent with TM. Tr. 32:5–6, 33:8–10; *see also* Pet'r's Ex. 5 at 162–64. His reference to M.P.'s abnormal CSF results to demonstrate a manifestation of extensive TM, strengthens Petitioner's theory of cause and effect. Tr. 33:8–11; *see also* Pet'r's Ex. 5 at 163. Dr. Steinman's reliance on M.P.'s imaging and clinical testing is evidence that she experienced an autoimmune response and neuroinflammation in her spinal cord. Such evidence is indicative of molecular mimicry and is probative.

Respondent's experts have been unable to persuasively refute Petitioner's presentation of a logical sequence of cause and effect in M.P.'s case. In fact, Dr. Gans cited to M.P.'s clinical testing and admitted that her platelet count from May 27, 2015, showed evidence of inflammation. Resp't's Ex. A at 3 (citing Pet'r's Ex. 5 at 9). Additionally, Dr. Kruer maintained that to prove causation, he would require evidence of an autoreactive response in M.P. to the specific proteins attacked in ADEM and TM, MOG and MBP. However, this is not the standard in the Program. *See, e.g.*, *Capizzano,* 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). He relied on the fact that M.P. was never tested or shown to have autoantibodies to these myelin proteins to argue there is no evidence of autoreactivity. *See* Tr. 120:19–25, 121:1–3; Resp't's Ex. C at 3. However, the medical literature contradicts Dr. Kruer's emphasis on the importance of autoantibodies to MOG and MBP to show an autoreactive response. The article by Ramanathan et al.[93] establishes that such autoantibodies are not conclusively known to cause disease even when they are present. *See* Resp't's Ex. C, Tab 13. Similarly, the articles by Ota[94] and Pette[95] show that "healthy people" can still have an immune response to myelin. Tr. 93–94; Pet'r's Exs. 58–59.

Dr. Steinman's theory that M.P.'s vaccinations and HMPV infection created a "perfect storm" is further supported by M.P.'s symptomology and clinical progression. On the day of vaccination, M.P. had a normal physical examination. Pet'r's Ex. 4 at 49–53. Within three days of her May 14, 2015 vaccinations, she developed a fever, cough, and runny nose. Such symptoms ceased prior to the start of M.P.'s vomiting on May 25, 2015, and her mobility issues wherein she refused to walk, seemed weak, and had diminished strength on May 26–27, 2015. *See id.* at 76–81. She was ultimately diagnosed with an HMPV infection and ADEM/TM on May 27, 2015. *Id.* at 80; *see also* Pet'r's Ex. 16 at 3.

Petitioner's support for *Althen* prong two is also based on M.P.'s treater's notation on causation. Dr. Freeland-Hyde wrote on June 8, 2015, that the "[e]tiology [for M.P.'s ADEM/TM is] unclear as [she] did test [positive] for [HMPV] and also received MMR/varicella vaccine[s] about [one and a half] weeks prior to [the] onset of [her] symptoms." Pet'r's Ex. 4 at 89. Dr. Steinman credibly testified that, to him, this notation meant that M.P.'s May 14, 2015 MMR and varicella vaccinations and her HMPV infection caused her injuries. Tr. 72–74. Such evidence, when taken together with M.P.'s medical record, provides additional support for vaccine-causation. In fact, Dr. Kruer conceded that, although rare and unlikely, it is "possible" that the MMR and varicella vaccines triggered M.P.'s ADEM and TM. Tr. 120:9–18, 123:21–23.

The evidence provided in this case, including M.P.'s clinical progression and testing, her treating physician's note, and Dr. Steinman's expert opinion, provide preponderant support for Petitioner's theory of cause and effect that is not based on a temporal association alone. *See Grant,* 956 F.2d at 1148; *see also Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983) (finding that "[w]ithout more, [a] proximate temporal relationship will not support a finding of causation"). In accordance with *Shyface*, I find it more likely than not that both M.P.'s HMPV infection and MMR and varicella vaccinations played a role in the development of her injuries. I find that but-for M.P.'s

[93] *See* S. Ramanathan, et al., *supra* note 79.
[94] *See* K. Ota, et al., *supra* note 30.
[95] *See* M. Pette, et al., *supra* note 31.

May 14, 2015 vaccinations, she would not have developed ADEM and TM. Petitioner has therefore satisfied prong two of *Althen*.

E. *Althen* Prong Three

Under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. For example, if a petitioner's theory involves a process that takes several days to develop after vaccination, an injury that occurred within a day of vaccination would not be temporally consistent with that theory. Conversely, if the theory is one that anticipates a rapid development of a reaction post vaccination, the development of the alleged injury weeks or months post vaccination would not be consistent with that theory. *See de Bazan*, 539 F.3d at 1352. Causation-in-fact cannot be inferred from temporal proximity alone. *See Grant,* 956 F.2d at 1148; *Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Hasler*, 718 F.2d at 205 ("[w]ithout more, [a] proximate temporal relationship will not support a finding of causation").

The parties generally agree that the timeframe for developing a demyelinating condition following vaccination is between one and fourteen days and up to several weeks post vaccination. *See, e.g.*, Pet'r's Ex. 19 at 28. This timeframe is well-supported by the medical literature. Petitioner's reliance on the Bennetto and Scolding[96] article, which shows that the onset of ADEM post vaccination can occur within one day and three weeks or more, is persuasive. Pet'r's Ex. 41 at 3. The article by Sapuan et al.[97] also indicates that ADEM "occurs a few days to several weeks after infections or vaccinations." Tr. 72:19–20; Pet'r's Ex. 32 at 1. Petitioner's position is further supported by the ADEM information page published by the Cleveland Clinic,[98] which notes the onset time for ADEM following vaccination ranges from seven to fourteen days. Pet'r's Ex. 30 at 1; Tr. 71:21–23, 72:2–6. While Petitioner's submitted medical literature and testimony do not address the post-vaccination onset time for the development of TM specifically, it does provide a timeframe for the onset of ADEM, which, as Dr. Steinman credibly explained, is "a similar phenomenon" to TM, wherein the immune system attacks the spinal cord. Tr. 39:24–25, 40:1; *see also e.g.*, *E.M.*, 2021 WL 3477837, at *42 (comparing the onset time of GBS via molecular mimicry to the timeframe for small fiber neuropathy, a comparable demyelinating condition). As M.P. suffered from both injuries, the medical literature provides support for the onset of her ADEM and TM via her proposed biological mechanism.

The record reflects that M.P. received MMR and varicella vaccinations on May 14, 2015, and the parties generally do not dispute that she experienced the onset of her ADEM and TM on May 27, 2015, approximately thirteen days later. This is supported by M.P.'s medical record and Dr. Steinman's credible testimony in which he explained that the first sign of a neurological complaint occurred on May 27, 2015, when M.P. "was very weak and refusing to walk." Tr. 31:17–21. Thirteen days fits "[v]ery comfortably[]" within the appropriate onset timeframe for M.P.'s conditions. Tr. 72:10–13.

[96] *See* L. Bennetto & N. Scolding, *supra* note 41.
[97] *See* S. Sapuan & H. Basri, *supra* note 53.
[98] *See supra* note 52.

I must note that Dr. Steinman put forth multiple, differing accounts of the amount of days between vaccination and the date of onset of M.P.'s symptoms. Dr. Steinman opined that the onset of M.P.'s symptoms occurred eleven days post vaccination in his reports and testimony. *See, e.g.*, Tr. 38:1. However, he testified that the onset of M.P.'s ADEM/TM was on May 27, 2015, with the first signs of neurological complaints, thirteen days post vaccination. *See, e.g.*, Tr. 31:17–21. He also wrote that the manifestation of M.P.'s ADEM and TM was on May 26, 2015. Pet'r's Ex. 21 at 1. These discrepancies are inconsequential because an eleven to thirteen-day onset time falls within the generally accepted timeframe for the onset of ADEM/TM post vaccination, as indicated by the medical literature.

I find that Petitioner has presented preponderant evidence to establish that the onset of M.P.'s ADEM and TM occurred in a timeframe consistent with Petitioner's proposed theory of causation. Therefore, Petitioner has satisfied her burden under *Althen* prong three.

F. Alternative Cause

If a petitioner presents a prima facie case, the Federal Circuit has held that the burden of proof shifts to the government, and Respondent must prove that the "'injury . . . described in the petition is due to factors unrelated to the . . . vaccine.' 42 U.S.C. § 300aa-13(a)(1)(b)." *Knudsen,* 35 F.3d at 547. "It is not enough for a factor unrelated to be a 'substantial cause' of the [P]etitioner's injury, but rather, the factor unrelated must be the sole substantial factor in bringing about the injury." 42 U.S.C.A. § 300aa-13(a)(1)(B); *see also Stone v. Sec'y of Health & Hum. Servs.,* 99 Fed. Cl. 187, 193 (2011); *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Hum. Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing § 13(a)(1)(B)). Special masters therefore must first consider whether a petitioner has satisfied his burden of showing a logical causal relationship between the vaccine he received and his sustained injury, and only then may shift the burden to the respondent to prove alternate causation by a preponderance of the evidence. *See Stewart v. Sec'y of Health & Hum. Servs.,* No. 06-777V, 2011 WL 3241585 (Fed. Cl. July 8, 2011). The Federal Circuit has made it clear that "the petitioner generally has the burden on causation, but when there are multiple independent potential causes, the government has the burden to prove that the covered vaccine did not cause the harm." *Walther,* 485 F.3d at 1151; *see also Sharpe v. Sec'y of Health & Hum. Servs.*, 964 F.3d 1072, 1083 (Fed. Cir. 2020) (finding that "the burden falls on the government under the 'factor unrelated' inquiry to show that the pre-existing condition caused the significantly worsened condition[]").

In this case, Petitioner has established a prima facie case for compensation under *Althen.* Therefore, Respondent has the burden to prove M.P.'s HMPV was responsible for her injuries. However, Respondent has not done so.

The literature cited by Respondent explains that an infection or illness has been associated with the development of severe reactions, including ADEM and TM. *See, e.g.*, Resp't's Exs. A, Tabs 12, 15–17; Resp't's Exs. C, Tabs 2–3, 6–7; Resp't's Ex. E at 1. Dr. Gans' testimony regarding the body of literature showing an association between HMPV infection and the development of CNS abnormalities is informative but not dispositive, as Petitioner does not dispute that HMPV can cause CNS abnormalities. *See* Resp't's Exs. A, Tabs 6–8, 11.

Instead, Respondent is attempting to establish alternate causation based on chronology alone. Respondent's experts relied on M.P.'s symptomology consisting of a runny nose, cough, and fever, which then progressed to neurological symptoms, to opine that such progression was consistent with a primary infection with HMPV in young children resulting in ADEM/TM. Resp't's Ex. A at 5; Resp't's Ex. C at 2. I am not persuaded by Respondent's interpretation of M.P.'s symptomology and clinical progression. The fact that M.P. experienced symptoms consistent with an HMPV infection post vaccination, which then progressed to ADEM/TM, does not support Respondent's position that M.P.'s HMPV infection alone, rather than the vaccines, caused her ADEM/TM.

Both of Respondent's experts were unable to parse out the effect of M.P.'s vaccinations compared to her HMPV infection. Dr. Steinman's testimony that he could not assign a statistical percentage to the likelihood of HMPV over the vaccinations as the cause of M.P.'s injuries, is both persuasive and consistent with Respondent's experts' testimony reflecting the same limitation. Respondent has therefore failed to show that M.P.'s HMPV infection was the sole cause of her ADEM and TM. As such, Respondent did not establish by preponderant evidence that M.P.'s ADEM and TM were caused by an alternate cause than her vaccinations.

V. Conclusion

Petitioner has failed to satisfy her burden for a Table claim of encephalitis. However, Petitioner has established by preponderant evidence that the MMR and varicella vaccines M.P. received on May 14, 2015, were the cause-in-fact of her ADEM and TM. Therefore, Petitioner has demonstrated entitlement to compensation. Accordingly, this case shall hereby proceed to the damages phase.

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master